TO EVALUATE THE EFFICACY OF DEEP INSPIRATIONAL BREATH HOLD TECHNIQUE AND ITS DOSIMETRIC ADVANTAGES OVER FREE BREATHING TECHNIQUE IN CARDIAC AND LUNG SPARING IN LEFT SIDED POSTMASTECTOMY CONFORMAL RADIOTHERAPY

Dissertation Submitted In Partial Fulfillment Of

MD BRANCH RADIOTHERAPY
EXAMINATION APRIL 2016

To

THE TAMILNADU Dr. M.G.R MEDICAL UNIVERSITY
CHENNAI – 600032

By

Dr ANUPAMA DARAPU

Post Graduate Registrar
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April 2016

CERTIFICATE

This is to certify that the dissertation entitled **"TO EVALUATE THE EFFICACY OF DEEP INSPIRATIONAL BREATH HOLD TECHNIQUE AND ITS DOSIMETRIC ADVANTAGES OVER FREE BREATHING TECHNIQUE IN CARDIAC AND LUNG SPARING IN LEFT SIDED POSTMASTECTOMY CONFORMAL RADIOTHERAPY"** is an original work by **Dr ANUPAMA DARAPU** in partial fulfillment towards MD Radiotherapy (Branch IX) Degree Examination of the Tamil Nadu Dr M G R Medical University to be held in April 2016.

GUIDE
Dr. Subhasini John,
Professor,
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CERTIFICATE

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Christian Medical College,
Vellore.

HEAD OF THE DEPARTMENT
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Professor and Head,
Department of Radiotherapy,
Christian Medical College,
Vellore.

CERTIFICATE

I **ANUPAMA DARAPU**, PG Registrar, Department of Radiation therapy, Christian Medical College Vellore hereby declare that the dissertation titled ***"TO EVALUATE THE EFFICACY OF DEEP INSPIRATIONAL BREATH HOLD TECHNIQUE AND ITS DOSIMETRIC ADVANTAGES OVER FREE BREATHING TECHNIQUE IN CARDIAC AND LUNG SPARING IN LEFT SIDED POSTMASTECTOMY CONFORMAL RADIOTHERAPY"*** is a bonafide work done by me for partial fulfillment towards MD Radiotherapy (Branch IX) Degree examination of the Tamil Nadu Dr M G R Medical University to be held in April 2016.

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July 11, 2014

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Effect of deep inspirational breath hold as compared to free breathing on doses to the heart, Left anterior descending coronary artery and lung for conformal post mastectomy radiotherapy of chest wall in left sided carcinoma breast patients.
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Dear Dr. Anupama Darapu,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Nihal Thomas, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Nihal Thomas
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Dear Dr. Anupama Darapu,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project entitled "Effect of deep inspirational breath hold as compared to free breathing on doses to the heart, Left anterior descending coronary artery and lung for conformal post mastectomy radiotherapy of chest wall in left sided carcinoma breast patients." on February 19, 2014.

The Committees reviewed the following documents:

1. IRB Application format
2. Curriculum Vitae' of Drs. Anupama Darapu, Subhashini John, Rajesh B, Patricia. S.
3. Informed Consent form (English, Bengali & Telugu)
4. Consent form (English, Bengali & Telugu)
5. No of documents 1-4

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The following Institutional Review Board (Blue, Research & Ethics Committee) members were present at the meeting held on February 19, 2014 in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore 632002.

Name	Qualification	Designation	Other Affiliations
Dr. Paul Ravindran	PhD, Dip RP, FCCPM	Professor, Radiotherapy, CMC, Vellore	Internal, Clinician
Dr. J. Visalakshi	MPH, PhD	Lecturer, Dept. of Biostatistics, CMC.	Internal, Statistician
Dr. Inian Samarasam	MS, FRCS, FRACS	Professor, Surgery, CMC	Internal, Clinician
Dr. Anup Ramachandran	Ph. D	The Wellcome Trust Research Laboratory Gastrointestinal Sciences, CMC, Vellore	Internal, Basic Medical Scientist
Dr. Jacob John	MBBS, MD	Associate Professor, Community Health, CMC, Vellore	Internal, Clinician
Dr. Niranjan Thomas	DCH, MD, DNB (Paediatrics)	Professor, Neonatology, CMC, Vellore	Internal, Clinician
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Dr. Anand Zachariah	MBBS, PhD	Professor, Medicine, CMC, Vellore	Internal, Clinician
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Mr. C. Sampath	B. Sc, BL	Legal Expert, Vellore	External, Legal Expert

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We approve the project to be conducted as presented.

CHRISTIAN MEDICAL COLLEGE, VELLORE

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1. I understand that the research grant is sanctioned only for the specific project approved by the Institutional Review Board and should be used exclusively for this project

2. I note that the project will become operational with effect from the date on which the grant is received, and I agree to complete it within the stipulated time of 15 months.

3. I agree to submit promptly and regularly, the periodical (Half Yearly for One Year Project/Annually for Two years project) reports and the final report of the work done, in the approved format.

4. If I plan to leave the institution before the completion of the project. I will submit a complete and detailed report of the work done by me on the project till the date of relief and transfer the project, either to the Guide or to the Co-Investigator for completion and submission of the Final Report.

5. I agree that any publication arising out of this project will carry an acknowledgement of the financial support of the Christian Medical College Fluid Research Fund

Fluid Grant Allocation:

A sum of Rs. 62,500/- (Rupees Sixty Two Thousand Five Hundred Only) will be granted for 15 months.

PRINCIPAL

D. Anu

Dr. Anupama Darapu
Radiation Oncology

Dr. Subhashini John
Radiation Oncology

Project Title: Effect of deep inspirational breath hold as compared to free breathing on doses to the heart, Left anterior descending coronary artery and lung for conformal post mastectomy radiotherapy of chest wall in left sided carcinoma breast patients.

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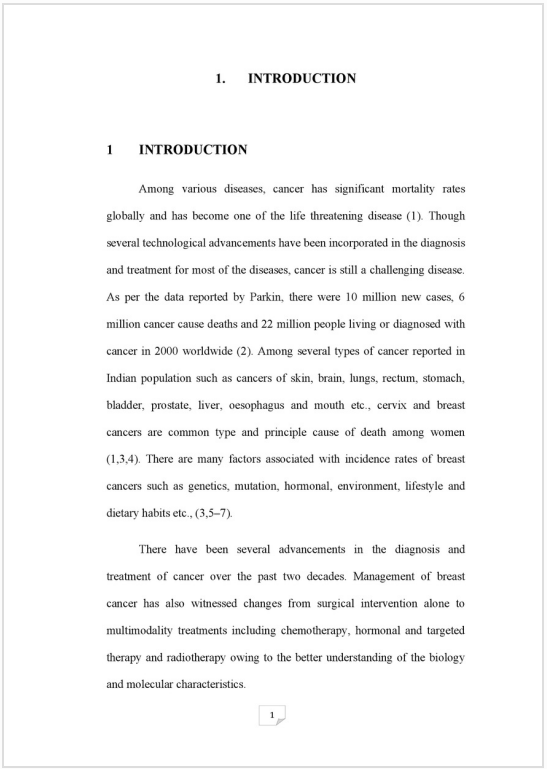

1. INTRODUCTION

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Among various diseases, cancer has significant mortality rates globally and has become one of the life threatening disease (1). Though several technological advancements have been incorporated in the diagnosis and treatment for most of the diseases, cancer is still a challenging disease. As per the data reported by Parkin, there were 10 million new cases, 6 million cancer cause deaths and 22 million people living or diagnosed with cancer in 2000 worldwide (2). Among several types of cancer reported in Indian population such as cancers of skin, brain, lungs, rectum, stomach, bladder, prostate, liver, oesophagus and mouth etc., cervix and breast cancers are common type and principle cause of death among women (1,3,4). There are many factors associated with incidence rates of breast cancers such as genetics, mutation, hormonal, environment, lifestyle and dietary habits etc., (3,5–7).

There have been several advancements in the diagnosis and treatment of cancer over the past two decades. Management of breast cancer has also witnessed changes from surgical intervention alone to multimodality treatments including chemotherapy, hormonal and targeted therapy and radiotherapy owing to the better understanding of the biology and molecular characteristics.

1

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ABSTRACT

BACKGROUND: To evaluate the efficacy of deep inspirational breath hold technique and its dosimetric advantages over free breathing technique in cardiac (heart and LAD) and ipsilateral lung sparing in left sided postmastectomy field in field conformal radiotherapy. DIBH is highly reproducible which arrest the respiratory motion provides clinical and dosimetric benefits over free breathing (FB).

MATERIALS AND METHODS: Nineteen left sided post mastectomy patients were immobilized using breast board with both the arms positioned above the head. For all the patents, two sets of planning CT images were acquired using Biograph true point HD CT scanner with the same setup, one with FB and the other during DIBH by tracking the respiratory cycles using Varian real time position management (RPM) system. The target (chest-wall and supraclavicular region), OARs (ipsilateral lung, contralateral lung, heart, LAD and contralateral breast) and other organs at interests were delineated as per the RTOG contouring guidelines. The single isocenter conformal field in field treatment plans were generated in the Eclipse treatment planning system in both FB and DIBH images and doses to the target and OARs were compared. The standard fractionation regimen of 50 Gy in 25 fractions over a period of 5 weeks was used for all the patients in this study.

RESULTS AND DISCUSSION: The target coverage parameters (V95, V105, V107 and D_{mean}) were found to be 97.8 ±0.9%, 6.1 ±3.4%, 0.2 ±0.3% and 101.9 ±0.5% respectively in FB plans and 98.1 ±0.8%, 6.1 3.2%, 0.2 ±0.3%, 101.9 ±0.4% in DIBH plans respectively. The plan quality indices CI and HI also showed 1.3 ±0.2 and 0.1 for FB plans and 1.2 ±0.3 and 0.1 respectively for DIBH plans. There was significant reduction in dose to heart in the DIBH plans compared to FB plans with p value nearly 0 for V5, V10, V25, V30 and D_{mean} dosimetric parameters.

The ipsilateral lung dose difference between FB and DIBH showed statistically significant p values and the difference in mean doses were found to be 7%, 15.7%, 11.8% and 10.7% in V5, V20, V30 and D_{mean} respectively. Significant reduction in dose to LAD in the DIBH plans compared to FB.

CONCLUSIONS: DIBH resulted in significant reduction in doses to the Heart, LAD and Lungs as with this technique there was an increase in distance between target and the OARs. With appropriate patient selection and adequate training, DIBH technique for radiotherapy to the chest is acceptable and achievable and therefore should be considered for all suitable patients as this could result in less radiotherapy related complications. However this technique is time consuming as the set up is complex, results in increased time for treatment delivery, needs patient co-operation and technical expertise.

LIST OF FIGURES

Figure 9 (A) The six marker neon localizer box with cross hairs and the goggle used in this study (B) Calibration setup with fixed couch vertical position using lasers.

Figure 10 (A) CT image in FB and DIBH (all view) of the patient ID 10

Figure 10 (B) Figure 10 (B) CT images of the patient with good performance

Figure 11 Location of heart at the reference plane in FB and corresponding plane on DIBH.

Figure 12 The mean heart distance from chest wall in FB and DIBH (at two planes)

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Figure 15 Differences in CI between FB and DIBH

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Figure 17 Difference in doses received by ipsilateral lung in FB and DIBH (A) V5 (B) V20 (C) V30 (D) D_{mean}

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Figure 19 Variation in V5 of contralateral lung in FB and DIBH

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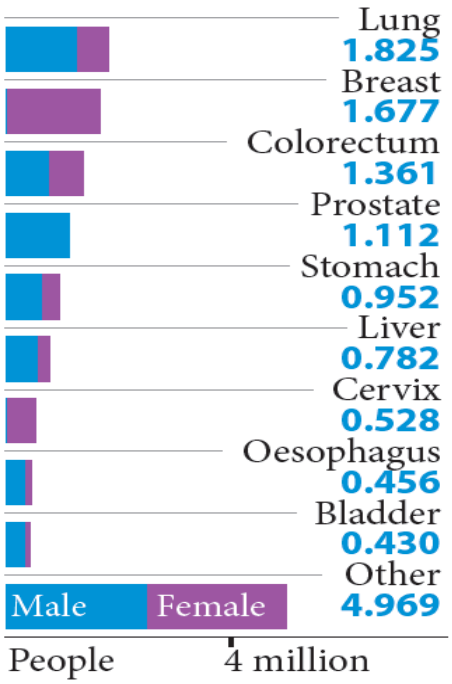
There have been several advancements in the diagnosis and treatment of cancer over the past two decades. Management of breast cancer has also witnessed changes from surgical intervention alone to multimodality treatments including chemotherapy, hormonal and targeted therapy and radiotherapy owing to the better understanding of the biology and molecular characteristics.

Radiotherapy in breast cancer has progressed from the use of conventional to conformal treatment techniques. Ever since its introduction into the management of breast cancer, radiotherapy has become an effective adjuvant treatment in achieving superior local control and also overall survival (8,9). However, there has been a risk of long term complications causing morbidity and mortality due to dose received by the underlying organs such as lungs and heart. Several studies have reported the correlation between the doses received by the heart and its effect in developing cardiac complications in the long term (10–12). There are studies which have reported that the cardiac toxicity was greater while delivering radiation therapy to the left sided breast cancer than the right (13–15). Hence efforts have been made in the planning techniques to decrease the doses to the heart and lungs without compromising on the target coverage. However, movement of chest wall due to breathing also accounts for variations in the doses delivered to the target and the OARs. Hence various methods have been developed to minimise this effect by using tumour tracking and deep inspirational breath hold (DIBH) while delivering radiation. In our study, we have done a dosimetric evaluation of DIBH technique in comparison with the free breathing to quantify the difference in the doses received by the OARs (heart, LAD and lungs) while delivering radiation to the left sided chest wall and supraclavicular region.

2. LITERATURE REVIEW

2.1 EPIDEMIOLOGY OF BREAST CANCER

According to GLOBOCAN 2012, an estimated 14.1 million new cancer cases and 8.2 million cancer-related deaths occurred in 2012, compared with 12.7 million and 7.6 million, respectively in 2008 (16). Owing to the considerable geographic changes in the incidence of cancers, breast cancer is common in developed countries than developing countries (4). According to world health organization (WHO), more than 1.2 million people are diagnosed with breast cancer worldwide every year, reported in the year of 2013 (6,17). Parkin reported breast cancer of about 1.05 million cases in the beginning of the last decade (2). The incidence and mortality of breast cancer has been increased by 20% and 14% respectively since the 2008 estimates. In fact, 1.7 million (i.e. 11.9% of total) women were diagnosed with breast cancer and it represents one in four of all cancers in women worldwide. Moreover, the incidence of breast cancer is rapidly increasing in India which was reported in the recent publication on Epidemiological correlates of breast cancer by Babu et al (5). The following are the details reported by international agency for research on cancer (IARC) (figure 1), WHO in 2014 (18).



Incidence is the absolute number of new cases arising in a given period (per year) in a specified population (per 100,000).

Figure 1 (A) Incidence of Cancer

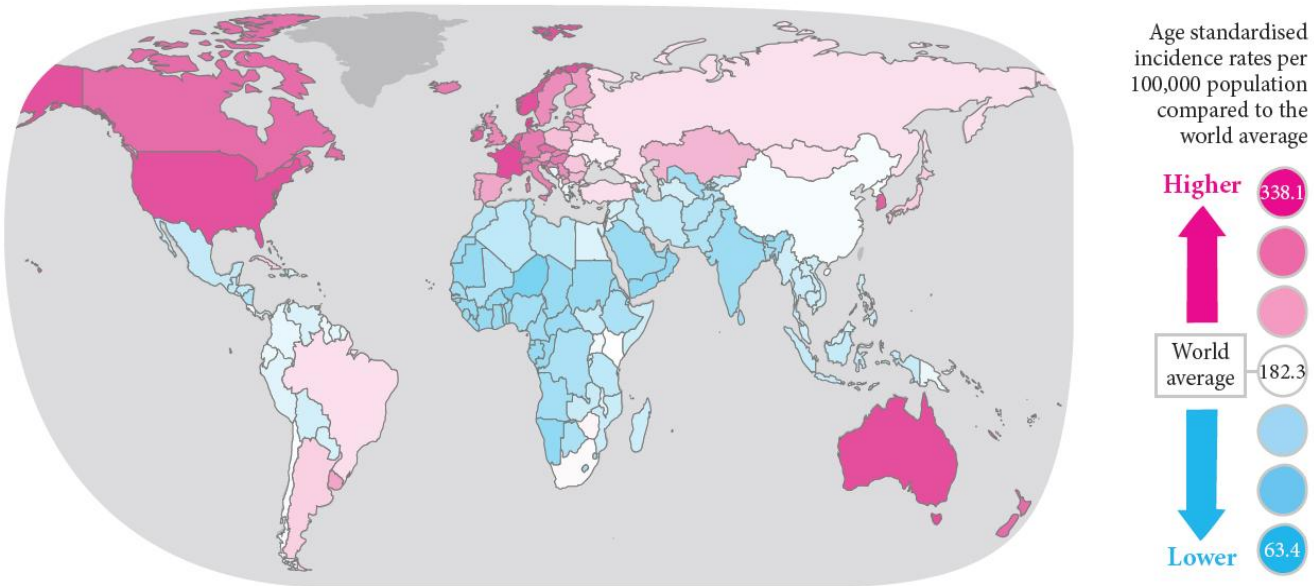
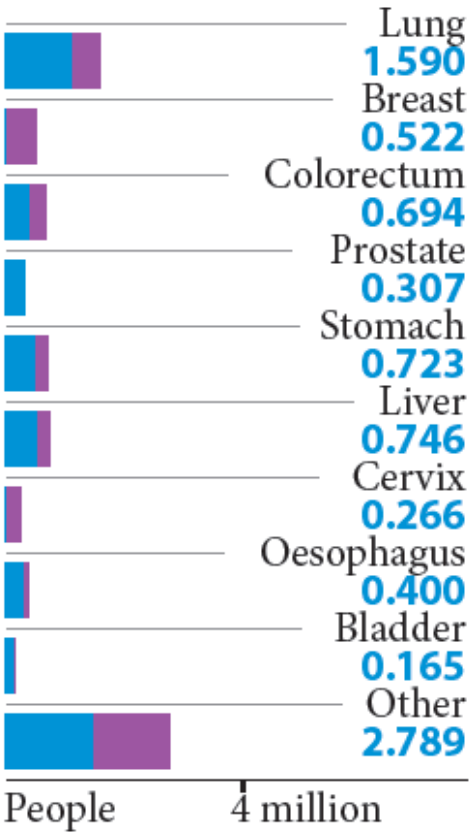


Figure 1 (B) Cancer Incidence by Country



Mortality is the absolute number of deaths occurring in a given period or per year in a specified population (per 100,000).

Figure 1 (C) Cancer Mortality

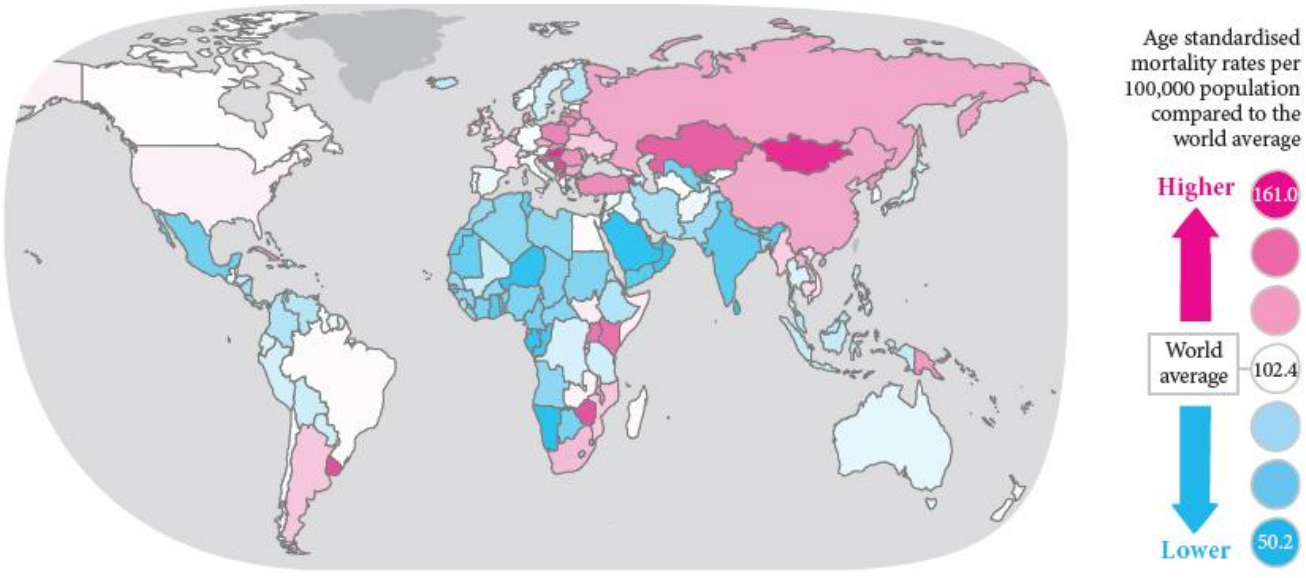


Figure 1 (D) Cancer Mortality by Country

The breast cancer was showed as most prevalent cancer by country among females, reported by the IARC, world cancer factsheet, WHO is shown below,

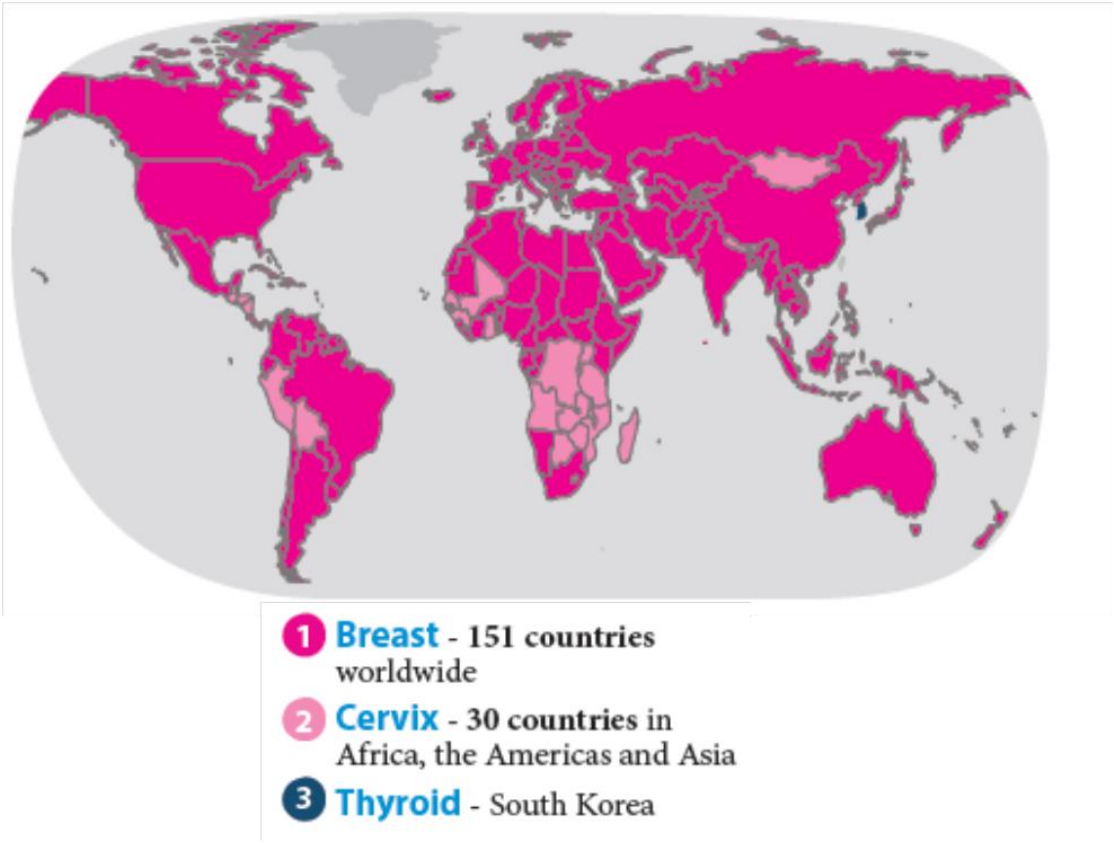


Figure 1 (E) Breast Cancer by Country

2.2 HISTORICAL BACKGROUND OF THERAPY

Breast cancer was described as early as 3000 BC by the Egyptians. Subsequently Greek and Roman physicians have written various articles about treatment of breast cancer (19). The management of breast cancer has changed from single modality (i.e. surgery) to multimodality which includes surgery along with chemotherapy and radiotherapy. Radiotherapy has been introduced in the treatment of breast cancer in the twentieth century when surgery for breast cancer had reached its limits and the efficacy of radical surgeries was re-evaluated by physicians for several reasons like inability to cure breast cancer by surgery alone, morbidity of radical surgery, combined modality like surgery and postoperative radiotherapy resulting in similar local control as radical surgery with less morbidity, introduction of chemotherapy leading to survival advantage, better understanding of biology of breast cancer and usage of variety of hormonal agents etc. In 1948, Robert Mc Whirter was the first person to report the benefit of radiotherapy in the treatment of nodal disease in breast cancer (19). Radiotherapy for breast cancer has progressed from the usage of kilovoltage superficial x-rays, orthovoltage to Megavoltage beams over time. These technological advancements have lead to a better local control by delivering higher doses to the target volume (chest wall and nodal regions). However, they have lead to a higher risk of developing long term morbidity and mortality due to cardiac and lung complications in view of the doses received by them (20). This has lead to further improvement in

radiotherapy planning and dose delivery with high precision radiotherapy techniques.

2.3 TREATMENT MODALITIES FOR BREAST CANCER

Treatment of breast cancer is multimodal and depends on several factors including the stage at presentation, patient related factors (age, patient preferences, general conditions etc.,), availability of services, physician expertise and socioeconomic factors. The various treatment modalities for breast cancer treatment are surgery, chemotherapy, radiotherapy, hormonal therapy and biological therapy.

2.3.1 ROLE OF SURGERY

Surgery is the main modality of treatment in breast cancer (21) which could be mastectomy or breast conservation surgery. In recent years, there is a paradigm shift from radical surgery to less invasive procedures like breast conservation surgeries and sentinel node biopsy, which are evolving as the standard of care (22). Most common type of surgery practiced in India for breast cancer is modified radical mastectomy due to various factors. These include, tumour factors (locally advanced nature of disease at presentation), patient factors [concern about disease free survival

than conservation of breast, finances - breast conservative surgery is relatively expensive than mastectomy), poor adherence to follow up regimes], physician factors (surgical expertise and availability of recourses for surgery) and access to radiotherapy equipment.

2.3.2 ROLE OF CHEMOTHERAPY

The goal of chemotherapy is to downstage the tumour when used in neoadjuvant setting and to decrease the chances of recurrence by eradicating micro-metastatic deposits. In addition, chemotherapy improves breast cancer outcome by preventing distant metastasis (23). Haagensen and Stout showed that there is need for other treatment modalities along with surgery for locally advanced breast cancer (LABC) from the outcome of clinical results of 74 patients who underwent radical mastectomy (24).

The radical mastectomy alone was not curative and incorporation of systemic chemotherapy along with surgery and radiotherapy improves overall survival and recurrence control (24–26). The similar outcome of induction chemotherapy results of National Surgical Adjuvant Breast Project (NSABP) for preoperative and postoperative breast cancers highlighted the breast conserving therapy (26). The substantial reduction of recurrence risk and significant proportional reduction in mortality rate among women (aged under 50 and those aged 50 to 69) showed absolute benefits of adjuvant chemotherapy (25).

2.3.3 ROLE OF RADIATION THERAPY

Radiotherapy (RT) had been shown to be effective in treating breast cancer in the early twentieth century. The rationale for postmastectomy radiation is prevention of local-regional recurrence (27). Findings of the 2005 Early Breast Cancer Trialists Group (EBCTCG) meta-analysis also showed the impact of improved local control on overall survival and showed that radiation therapy after breast conservation improved five year local control rates and also overall survival (28). In 1977, the Danish Breast Cancer Cooperative Group (DBCCG) suggested national guidelines for the first time regarding adjuvant radiotherapy for breast cancer (29,30).

The benefit of postmastectomy radiotherapy was first demonstrated by three randomized trials done between 1997 and 1999 in which patients who received adjuvant postmastectomy radiotherapy had statistically significant survival benefit when compared to those who did not receive the same (9,31). There would be a risk of local recurrence even after postmastectomy and various trials and metaanalysis have proven the advantage of adjuvant radiation in terms of reducing local recurrences and long term mortality due to breast cancer (9,28,31–33).

2.4 DIFFERENT TECHNIQUES OF EXTERNAL BEAM RADIATION THERAPY FOR BREAST CANCER

External Beam radiotherapy is grossly includes two types – Conventional and Conformal. The two dimensional Conventional radiotherapy (2DRT) makes use of regularly shaped, two to four equally weighted tangential beams with simple arrangements while conformal radiotherapy such as 3DCRT, IMRT (forward and inverse planning IMRT), IGRT, SBRT, Tomotherapy, volumetric arc therapy uses irregularly shaped, unequally weighted, multiple beam arrangements .

2.4.1 TWO DIMENTIONAL CONVENTIONAL RADIATION THERAPY

The conventional (2D) treatment planning consists of standardized treatment techniques making use of an x-ray simulator which simulates the functions and motions of the treatment unit and a 2D computer planning system which is used for dose calculation and to generate a dose distribution. In order to reduce the doses to the heart and lungs in conventional radiotherapy, parallel opposed tangential beams are used. More often the half beam blocked tangential beam technique is used. The patient is immobilised on a breast board and aligned by the help of two lateral lasers and an anterior laser. The field borders are fixed according to

the anatomical landmarks and adding margin to the field to account for penumbra as well as setup uncertainties. Additional margin to the field is given anteriorly to account for breathing movement.

In addition, the parameters such as central lung distance (CLD), maximum lung distance (MLD), average lung distance (ALD) and maximal heart distance (MHD) are also considered and the field borders are adjusted accordingly to ensure better target coverage and also to reduce the doses to the lungs and heart which will predict the probability of radiation induced pneumonitis and cardiac toxicity (34,35). The figure 2 shows the CLD and MHD in a simulator film.

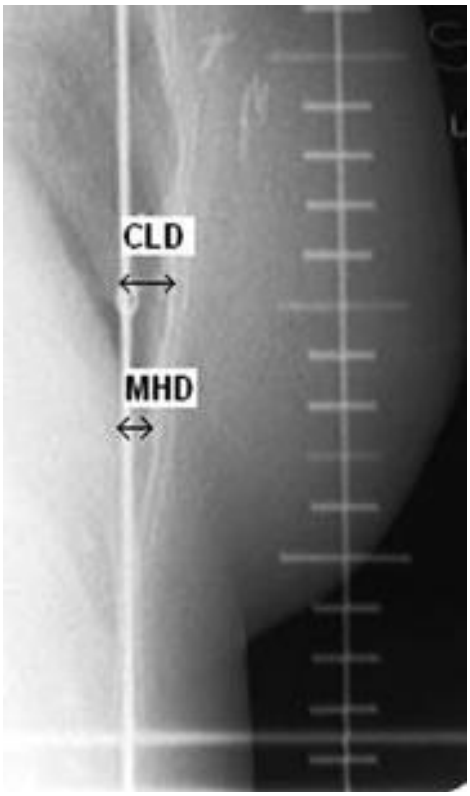


Figure 2 Simulator Film with CLD and MHD Marking (Courtesy: Practical Radiotherapy Planning by Jane Dobbs).

2D planning system generates dose distribution only in a single or few planes which could lead to treatment inaccuracy and thereby limiting its usage. The primary obstacles to achieve the maximum possible therapeutic advantage when the patient is being treated with conventional radiotherapy are the following:

- Uncertainties in the actual spatial extent of the target
- Inadequate knowledge of the special location and accurate shapes of OARs
- Unavailability of appropriate devices for conformal treatment planning and delivery
- limitations of computing desirable isodose distribution with the existing methods (36)

The advent of computed tomography (CT) and magnetic resonance imaging (MRI) and its incorporation in the planning and treatment has lead to better localisation of the tumour and has led to the development of conformal radiotherapy.

2.4.2 THREE DIMENTIONAL CONFORMAL RADIATION THERAPY

Three-dimensional conformal radiation therapy (3DCRT) is a technique where irregularly shaped beams are used in different projections

to match the size and shape of the tumour. This can be achieved by multileaf collimators which are independently moving banks of leaves attached in the treatment head of a linear accelerator (37). In conventional radiotherapy, the height and width of the tumour are matched with regularly shaped square or rectangular fields in which there is a chance of more healthy tissue being exposed to radiation. Advances in imaging technology such as CT, MRI, PET (Positron Emission Tomography) and SPECT (Single photon emission Computer tomography) have made it possible to locate and treat the tumour more precisely. CT images are used in computerized treatment planning systems (TPS) for dose calculation (38) which provide three dimensional anatomical details and tissue density information as arbitrary number (correspond to linear attenuation value) called Hounsfield units. 3DCRT uses the three dimensional projection images of the CT to focus precisely on the target with different gantry direction, while avoiding OARs and healthy surrounding tissue. Figure 3 shows the irregularly shaped MLC, beams eye view of target and OARs and dose distribution on CT image of 3D breast radiotherapy.

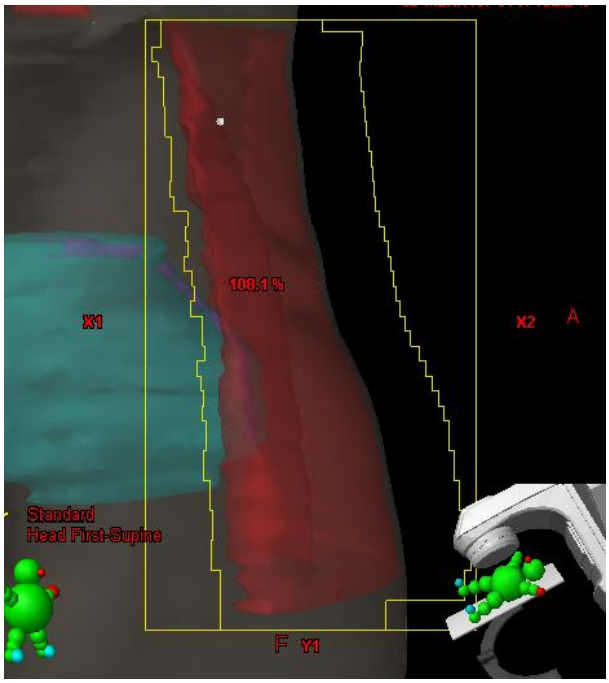


Figure 3 (A) Irregularly shaped BEV of the tangent beam

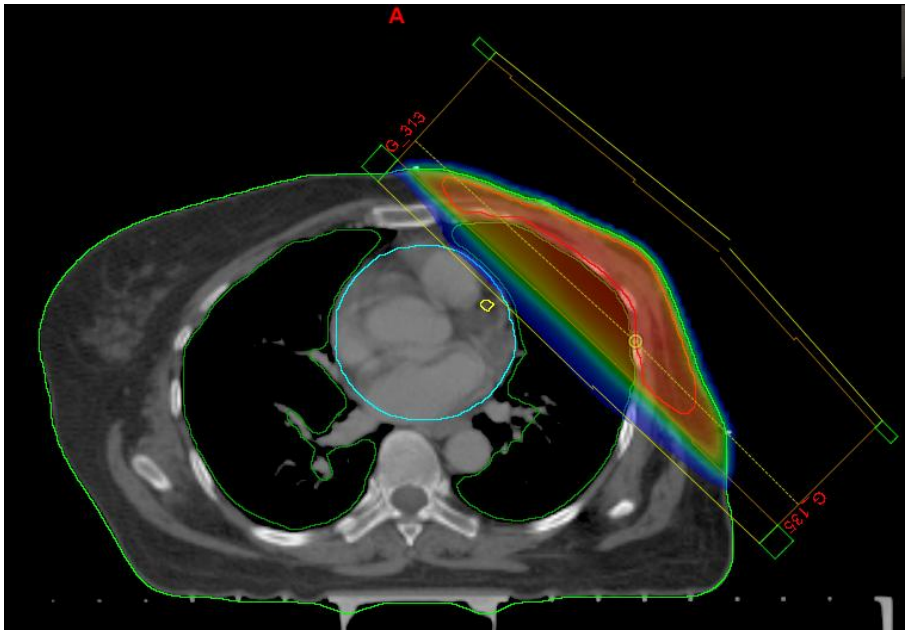


Figure 3 (B) Isodose Distribution of 3DCRT Plan with Tangential Beams

2.4.3 INTENSITY MODULATED RADIATION THERAPY

Intensity-modulated radiation therapy (IMRT) is an advanced form of 3DCRT. It uses sophisticated treatment planning software and hardware to vary the shape and intensity of radiation beam delivered to different parts of the patient body. IMRT is the most precise form of external beam radiation therapy and suitable treatment option for many sites such as head and neck, prostate cancer and breast cancer etc. IMRT permits treatment with rapidly varying intensity or fluence across fields that can be optimized to fit to the complex target volume defined by the physician, resulting in improved dose conformity and avoidance of critical structures (39,40). Several IMRT techniques were reported in radiotherapy in last two decades, differing in method of plan optimization and dose delivery (41). However, the MLC based IMRT techniques such as inverse planned IMRT (step and shoot or dynamic) and static or forward planned IMRT are widely used for treatment of breast radiotherapy. IMRT treatment offers fewer side effects than 3DCRT, but generally takes more time for planning and to deliver the desired dose.

2.4.3.1 INVERSE PLANNED IMRT

In inverse planned IMRT, the physician designates patient specific dose constraints to the target, OARs and surrounding normal tissues in the optimization process as expected input (39). In this method,

the sophisticated computerized treatment planning software is used to develop an individualized plan to meet the target and OAR dose constraints by allowing various intensity levels of radiation beam with different gantry angles. This process is termed inverse treatment planning. Figure 4 shows the inverse planned IMRT dose distribution for left sided breast radiotherapy plan.

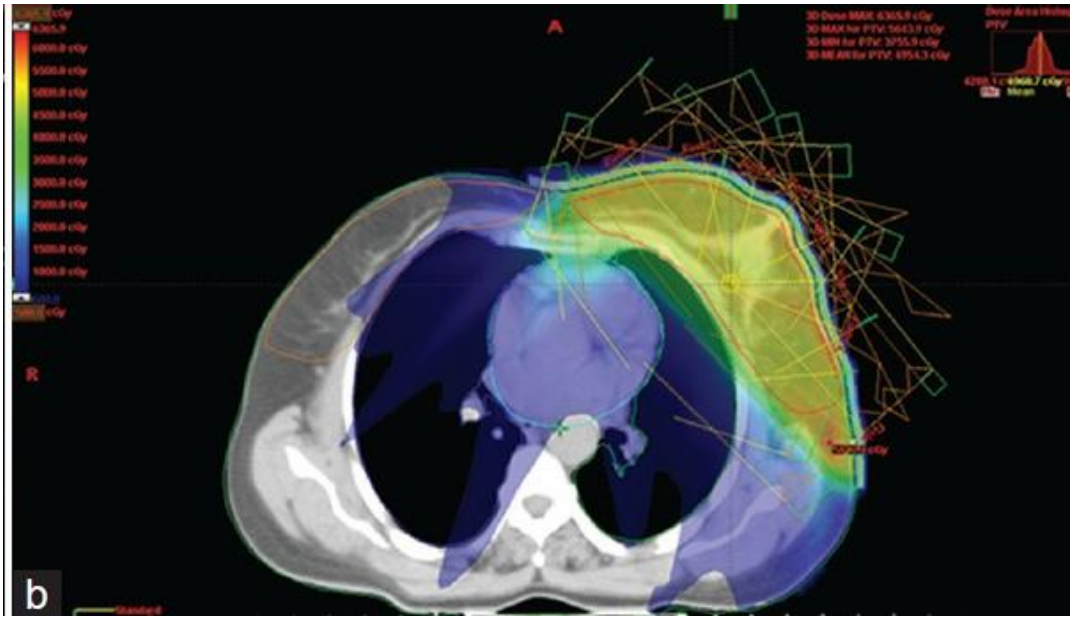


Figure (4) Inverse Planned IMRT Dose Distribution for left sided breast cancer.

2.4.3.2 FIELD IN FIELD OR FORWARD PLANNED IMRT

Unlike inverse planned IMRT, Field in field (FiF) or forward planned IMRT has 2 or more lower weighted sub fields or segmented fields which is created from the primary fields to shield the high dose region and increase the dose at cold spots in the target (42). FiF treatment plans does not require a pre-treatment quality assurance like inverse planned IMRT (43). FiF plans allow homogeneous dose distribution across the target volume than 3DCRT (44) and inverse planned IMRT, resulting in significant reduction in hotspot (lower maximum dose) (105%, 107% and 110%) and cold spot region within the target (higher minimal dose) (45–47). Figure 5 shows the sub fields used to shield the high dose in a FiF plan.

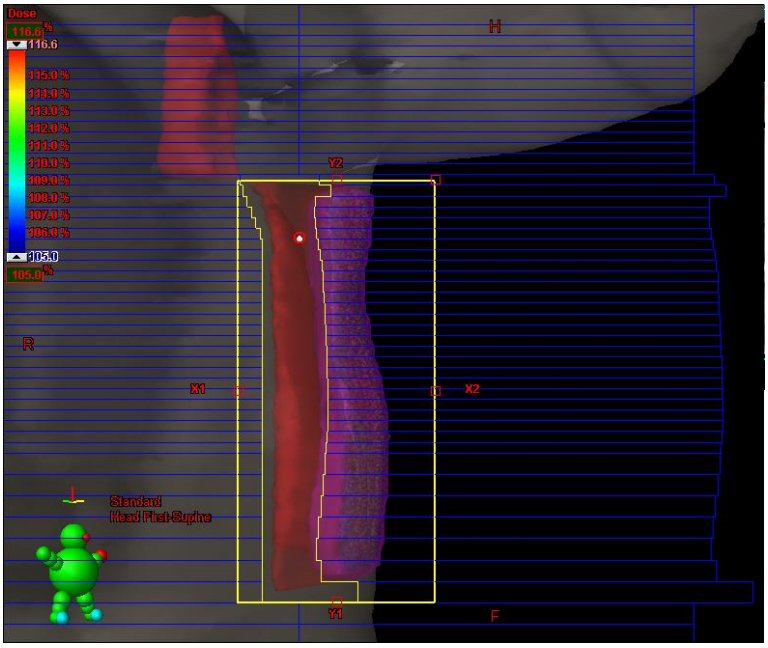
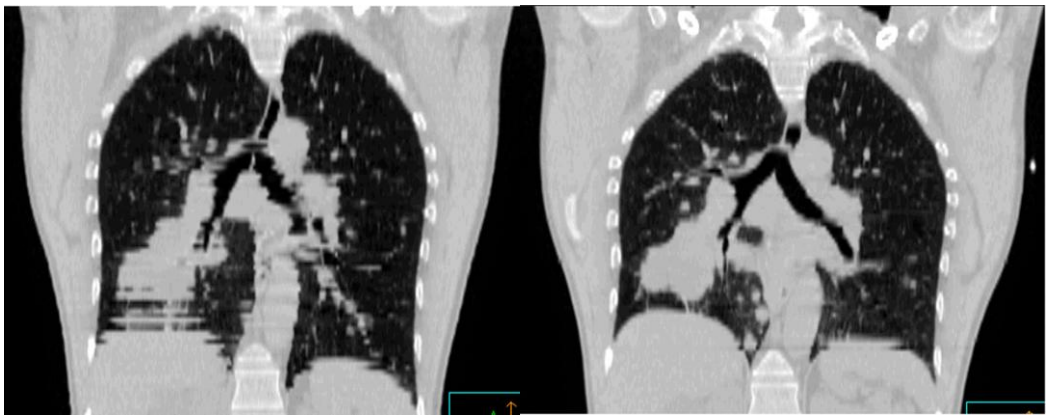


Figure 5 BEV of partially shielded sub-filed in FiF plan to block 105% isodose (magenta coloured).

2.5 EFFECT OF RESPIRATORY MOTION IN RADIATION THERAPY FOR BREAST

Respiratory, cardiac and gastrointestinal systems effect the movement of the target during radiotherapy among which respiratory motion has a significant effect on the intra and inter fractional delivery of radiotherapy to the chest or abdomen (48). Respiratory motion also causes artefacts during image acquisition which leads to distortion of the tumour volume and incorrect spatial representation of the anatomical structures (49,50). Figure 6 A and B shows CT scan images of thoracic region (coronal view) of a patient during free breathing and deep inspirational breath hold.



(A) ***(B)***

Figure 6 CT images (coronal view) of thoracic region of a patient during free breathing *(A)* and deep inspirational breath hold *(B)*. Courtesy: Managing Respiratory Motion in Radiation Therapy, Keall P and Mageras G, AAPM TG 76 2004.

Hence efforts have been made to account for and counteract the same. The following methods/techniques were described for management of respiratory motion during radiotherapy (48,49).

A. Respiratory gated techniques

B. Motion encompassing methods

C. Respiration synchronized techniques

D. Forced shallow breathing methods

E. Breath hold techniques

A. RESPIRATORY GATED TECHNIQUES

Respiratory gating denotes the acquisition and delivery of radiation (during imaging and treatment) during a specific phase of the respiratory cycle, often referred as 'Gate'. By monitoring the patient's respiratory cycle using either external or internal signals (with infrared camera or fiducial markers), the width and position of the gate can be determined (49,51). The Varian Real-time Position Management (RPM) system is the only commercially available software used for respiratory gated therapy and the same has been used in our study.

B. MOTION ENCOMPASSING METHODS

As there will be movement of the target and other structures due to breathing during delivery of radiation, estimation of the range of motion and the mean position of the target during imaging is important. The techniques available to include the range of tumour motion during imaging are,

I. Slow CT
II. Inhale and Exhale breath hold CT
III. 4D CT

Though these methods account for respiratory movement during imaging, there is a possibility of increased radiation exposure to the patient if not performed well.(48, 51–54)

C. RESPIRATION SYNCHRONIZED TECHNIQUES

Respiratory synchronized or real time tracking technique is one of the effective methods to dynamically accommodate respiratory motion by shifting or sweeping the beam in space to synchronize with normal respiratory cycle which make use of 100% duty cycle during dose delivery. This technique is less practised due to limited experience and technical expertise (49,56,57).

D. FORCED SHALLOW BREATHING METHODS

This technique was developed by Lax and Blomgren at Karolinska Hospital in Stockholm, to reduce the magnitude of the intra fractional motion during SBRT of lung and liver tumours. A stereotactic body frame equipped with the pressure plate (this equipment commercially produces by Elekta medical systems) used in this technique to minimize the diaphragmatic excursions, there by controlling the gas exchange during free breathing. Though several groups were studied the accuracy and reproducibility of this equipment, Negoro et al reported the most

comprehensive method (58,59). This method is not in much practise for breast radiotherapy.

E. BREATH HOLD METHODS

There are three types of breath hold methods such as Active Breathing Control (ABC), Self-held breath-hold, Self-held breath-hold using an External Marker and Deep inspirational breath hold.

I. ABC METHOD

ABC method was developed at William Beaumont Hospital and commercialized by Elekta, Inc. as the Active Breathing Coordinator (48). This method facilitates reproducible breath-hold technique in which the patient does not require to hold the breath with maximum inspiration capacity (60–62). Any pre-determined phase at active inspiration or along the free breathing cycle can be suspended by ABC apparatus. Figure 7 shows the Elekta's ABC system.

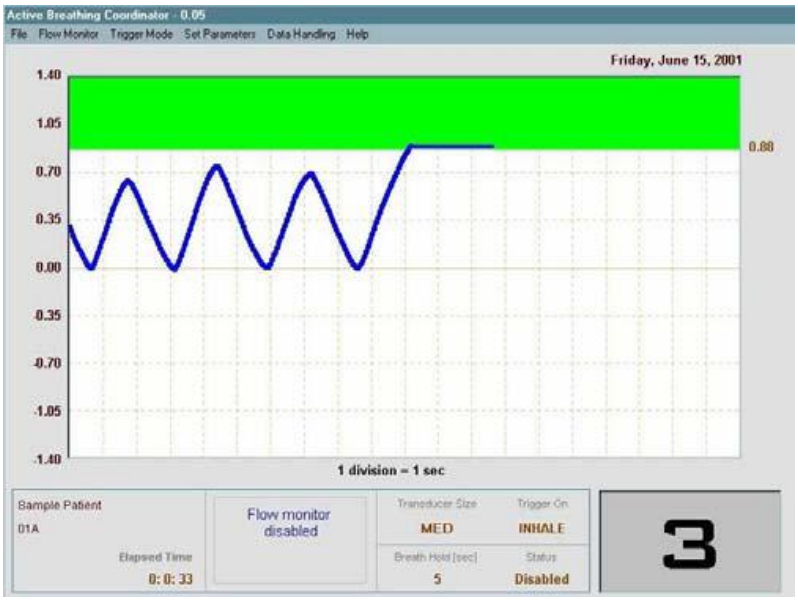


Figure 7 The Elekta's ABC system. Courtesy: Managing Respiratory Motion in Radiation Therapy, Keall P and Mageras G, AAPM TG 76 2004.

II. SELF-HELD BREATH-HOLD

In self breath hold technique, the patient holds the breath at some point in the breathing cycle and the beam will be turned on when the patient holds the breath. It makes use of Customer Minor (CMNR) interlock circuit where the patient can turn off the beam. Deep inspiration or expiration has proven to be most reproducible positions than any other phase of respiration as per several studies. Further, deep inspirational breath hold has further advantage of increasing the lung volumes significantly (48,49,55,63). In our

study, we have compared the differences in lung volumes between FB CT and DIBH CT.

III. SELF-HELD BREATH-HOLD USING AN EXTERNAL MARKER

In this technique, patients are instructed to hold their breath in specific phase respiratory cycle. There are two advantages in this technique such as Fastest dose delivery (~100 MU per 10 seconds breath hold using 600 MU/min dose rate while same dose delivery would take 30 seconds in FB technique) and Constant observation (constantly monitor the patient's respiratory cycle using a external fiducial marker which disable the beam if the patient fail to hold the breath in a specific phase of respiratory cycle) (48,49).

IV. DEEP INSPIRATIONAL BREATH HOLD

DIBH is most reproducible and controlled breathing technique under supervision during treatment, originally developed for treatment of lung cancers to reduce the PTV margin (1 to 2 cm) there by increasing the dose escalation while maintaining the same normal tissue complication probability (NTCP) (51,64,65). Studies proved that the heart moves away from the chest wall during DIBH. Remouchamps *et al* showed significant reduction in heart and lung doses by adapting the DIBH technique along

with ABC apparatus (66). Further, it showed as a more efficient and feasible technique to reduce the respiratory motion effectively and spare the normal tissue by increasing the lung volume (51) and also reduce the late cardiac toxicities associated with radiotherapy (67). The reproducibility of DIBH was reported by Hanley *et al* in which the average intra and inter breath hold deviation of 1 mm and 2.5 mm respectively (ranging from 0.5 mm to 4.9 mm) for lung-diaphragm boundary position while 26.4 mm was the deviation in normal breathing for the same (64). In order to reduce the risk of cardiovascular morbidity and mortality, the goal of reduction of dose-volume irradiation to the heart has become common in breast radiotherapy. Ha Yoon Lee *et al* reported the feasibility of DIBH in daily practice and potential reduction in radiation to the heart and LAD for left sided breast cancer (60). Similar study was also reported by Hayden *et al* in which he showed significant reduction in dose to heart and LAD in DIBH technique than FB (68). Feasibility and setup variability of fluoroscopy guided DIBH irradiation for left sided breast cancer was reported by Borst *et al*. He showed lower heart dose in comparison with FB and small setup variability (which did not affect the dose delivery to the chest wall) (69). Latty *et al* evaluated several DIBH techniques and showed the need for an optimum protocol for patient training and treatment evaluation, in order to achieve the accurate treatment delivery. The reproducible state of DIBH is beneficial to patients undergoing breast and thoracic radiotherapy; it significantly reduces respiratory motion and protects critical normal tissues.

Several methods for implementing DIBH have been developed and are described in this report. All the methods require patient compliance, active participation and, often, extra therapist participation.

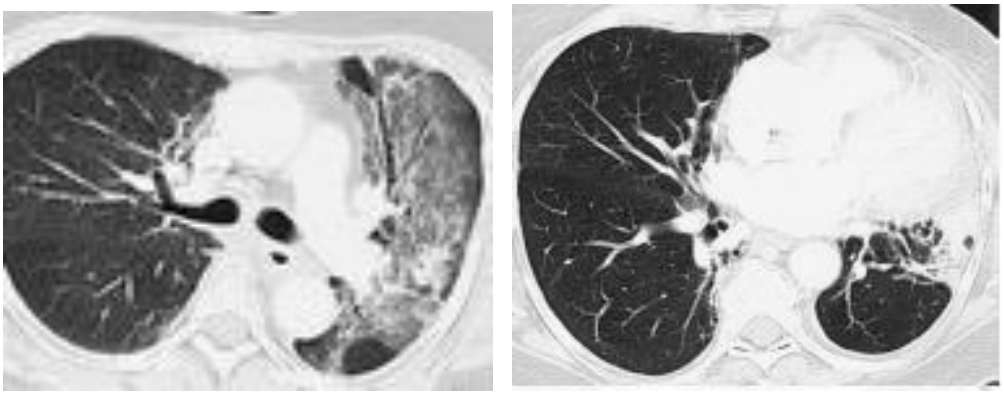
2.6 OARs IN POST-MASTECTOMY RADIOTHERAPY AND RADIATION INDUCED SIDE EFFECTS

A. LUNGS

Radiation induced lung disease (RILD) is a common complication of radiotherapy to the chest wall. It includes acute and late phases which correspond to radiation induced pneumonitis and radiation fibrosis respectively, as shown in figure 8. The risk of developing RILD depends on various factors like the total dose of radiation given (rare below 20 Gy, common above 40 Gy), fractionation, prior chemotherapy (Actinomycin D, Adriamycin, Bleomycin) (70). Table 1 shows the RTOG Acute Radiation Morbidity Scoring Criteria for lung.

Table 1 Acute Radiation Morbidity Scoring Criteria for lung - RTOG

Grade	Signs and Symptoms
0	No change
1	Mild symptoms of dry cough or dyspnoea on exertion
2	Persistent cough requiring narcotic, antitussive agents/ dyspnoea with minimal effort but not at rest
3	Severe cough unresponsive to narcotic antitussive agent or dyspnoea at rest/ clinical or radiologic evidence of acute pneumonitis/ intermittent oxygen or steroids may be required
4	Severe respiratory insufficiency/ continuous oxygen or assisted ventilation



(A) **(B)**

Figure 8 Radiation induced pneumonitis (A) and fibrosis (B)

B. HEART

Postmastectomy radiotherapy to the left chest wall invariably leads to exposure to the heart to radiation and hence the occurrence of long term complications. Even though the doses received by the heart could be significantly reduced due to modern radiotherapy techniques, several studies have shown that the average dose received by the heart is about 1 to 5 Gy. Exposure of this doses can cause ischemic heart disease, though the risk of development is uncertain and depends on presence of other cardiac risk factors (71). Table 2 shows the RTOG grading of cardiac morbidity due to radiation. The spectrum of radiation induced cardiac damage can range from Asymptomatic Coronary artery disease to sudden death (Table 3).

Table 2 Acute Radiation Morbidity Scoring Criteria for Heart - RTOG

Grade	Signs and Symptoms
0	No change over baseline
1	Asymptomatic but objective evidence of EKG changes or pericardial abnormalities without evidence of other heart disease
2	Symptomatic with EKG changes and radiologic findings of congestive heart failure or pericardial disease/ no specific treatment required
3	Congestive heart failure, angina pectoris, pericardial disease responding to therapy
4	Congestive heart failure, angina pectoris, pericardial disease, arrhythmias not responsive to non-surgical measures

Table 3 The spectrum of radiation induced heart disease

<table>
<tr><th>Radiation-induced atherosclerosis</th><th>Pericardial disease</th><th>Myocardial and Endocardial disease</th><th>Conduction disturbances</th><th>Valvular disease</th></tr>
<tr><td rowspan="2">Symptomatic</td><td>Acute pericarditis</td><td rowspan="2">Pancarditis</td><td rowspan="2">RBBB</td><td rowspan="3">-</td></tr>
<tr><td>Delayed pericarditis</td></tr>
<tr><td rowspan="2">Asymptomatic</td><td>Pericardial effusion</td><td rowspan="2">Cardiomyopathy</td><td rowspan="2">Atrioventricular nodal block</td></tr>
<tr><td>Constrictive pericarditis</td></tr>
</table>

Courtesy: Radiation Induced Heart Disease, A Clinical Update Yusuf et al, Cardiology Research and Practice, 2011.

C. LEFT ANTERIOR DESCENDING ARTERY (LAD)

LAD is one of the major coronary arteries supplying the anterior part of heart especially the ventricles and is the most common artery involved while delivering radiation to the left chest wall and the nodal regions as it is mostly received by the anterior part of the heart where the LAD is located. Doses received by the LAD are directly proportional to the risk of development of radiation induced ischemic heart disease hence studies have been done to quantify the doses received by LAD and its impact on development of cardiac morbidity.(72,73)

D. CONTRALATERAL BREAST

In the patients with breast cancer, there is a risk of development of malignancy in contralateral breast owing to various causes like genetic predisposition, tumour related factors like the histology, receptor status etc., The incidence has significantly decreased which can be attributed to the effective adjuvant therapies. However there exists a slight risk of development of second malignancy in the contralateral breast after receiving radiation for breast cancer. Considering a 55 year old healthy lady and a lady of the same age who is a breast cancer survivor, the risk of developing breast cancer would be 2.5% and 10 – 15 % respectively. But only a small percent

of this is attributed to the treatment and the risk after radiotherapy is mostly due to the scattered doses.(74,75)

3. AIMS AND OBJECIVES

AIM

To evaluate the efficacy of deep inspirational breath hold technique and its dosimetric advantages over free breathing technique in cardiac (heart and LAD) and ipsilateral lung sparing in left sided postmastectomy field in field conformal radiotherapy.

OBJECTIVES

To study the effect of deep inspirational breath hold on doses to the Heart, Left anterior descending coronary artery (LAD) and Lung for conformal postmastectomy radiotherapy to the chest wall in left sided carcinoma breast patients.

To compare the doses received by organs at risk the heart, LAD and lung during radiotherapy for post mastectomy left sided carcinoma breast during free breathing versus deep inspirational breath hold.

SECONDARY OBJECTIVE

To assess the feasibility of deep inspirational breath hold CT scan.

NULL HYPOTHESIS

There is no significant difference in doses received by the heart, LAD and lung in free breathing versus deep inspirational breath hold.

RELEVANCE OF THIS STUDY

1. Documentation and quantifying the influence of deep inspirational breath hold on doses received by the heart and LAD
2. It will aid in decision making, regarding treating the patients in deep inspirational breath hold in order to reduce the doses of radiation to the organs at risk without compromising on the dose to the target.

INCLUSION CRITERIA

1. Women with left sided breast cancer who require postmastectomy radiotherapy to chest wall and supraclavicular region

2. Patients who consent for undergoing CT scan in deep inspirational breath hold in the same setting and use of images for study purpose

EXCLUSION CRITERIA

1. Persons who cannot hold breath due to any reason

2. Patients who had primary or secondary flap reconstruction

SETUP UNCERTAINTY FACTORS

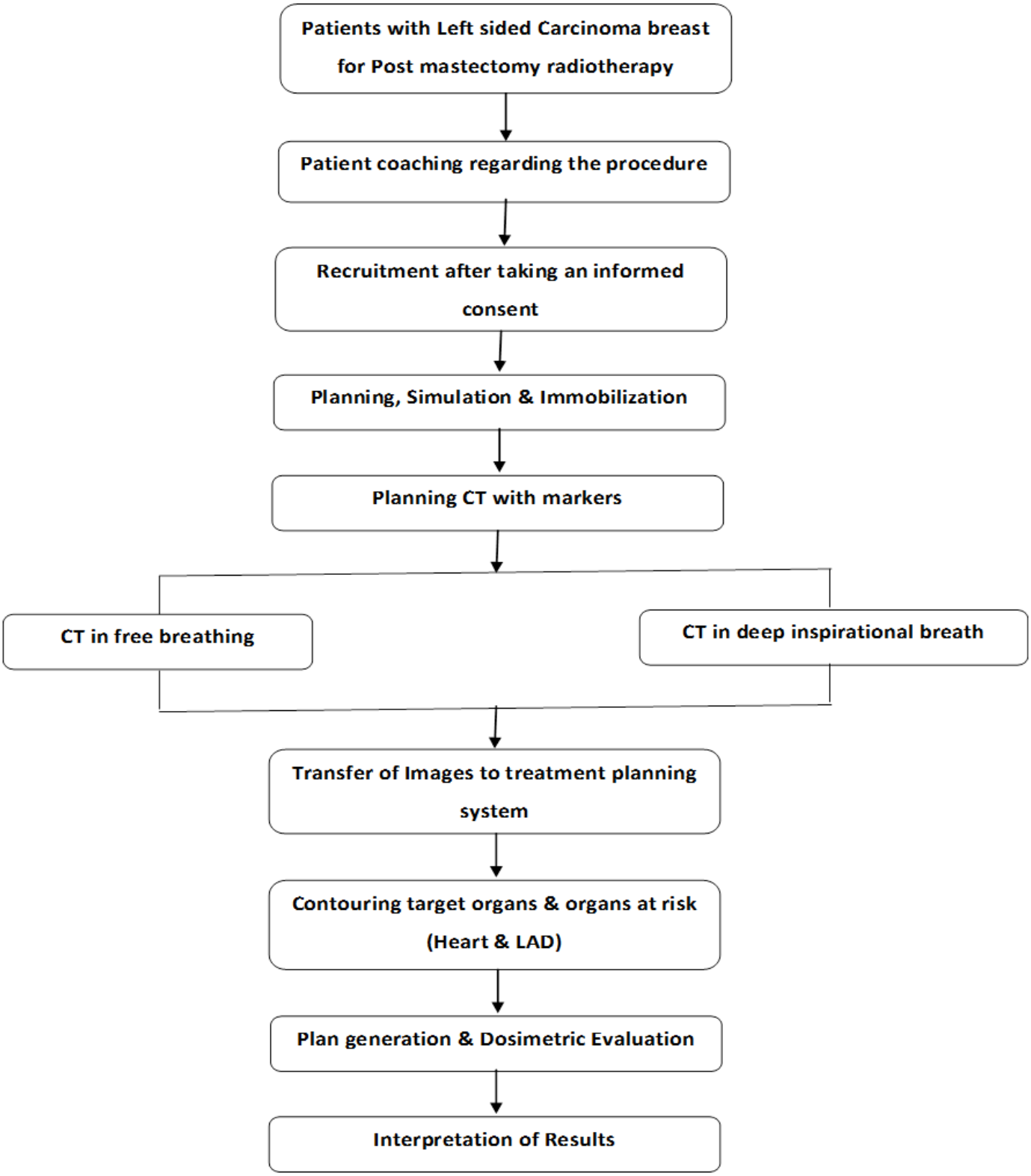
1. Height
2. Weight
3. Body mass index

PATIENT EVALUATION PARAMETERS

S.No	Variables	Parameters	Threshold / Limits/Sources
1	Age	< 40 years 41 to 55 years > 55 years	Lower Limit Normal Upper Limit
2	BMI	< 19 kg/m2 19 to 25 kg/m2 25 to 30 kg/m2 > 30 kg/m2	Under Weight Average Over weight Obese
3	Lung Volume	cubic centimetres	-
4	Heart distance from the CW	centimetres	-

4. MATERIALS AND METHODS

DIAGRAMMATIC ALGORITHM OF THE STUDY

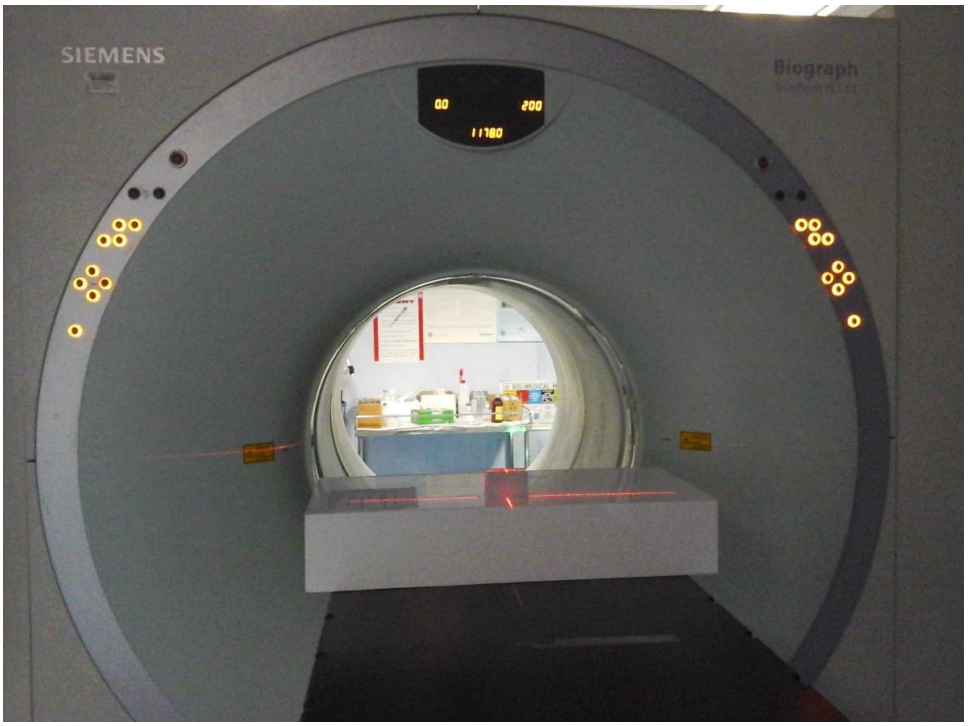


The patients undergoing post mastectomy radiotherapy for left sided breast cancer were recruited for this study after signing the consent form. Baseline ECHO and Pulmonary function tests were done. All the patients were well explained about the DIBH technique. They were trained regarding the same and were instructed to practice it for atleast a period of three days before undergoing planning CT scan.

4.1 CALIBRATION OF TRACKING SYSTEM

Calibration of infrared (IR) camera system (Varian medical system, USA) was performed prior to acquisition of the images. Figure 9 shows the six marker neon localizer box, video assisted goggles and the calibration setup of the IR camera,. Initially, the localizer box was kept on the calibration test tool at isocenter position using lasers. It was followed by a 10 step calibration procedure using Varian RPM software by placing localizer box at various positions on the test tool with fixed table vertical position (ideally at 200) and three different longitudinal position to account for the coordinates of the various table position during CT scan. For each patient, the calibration check was performed to verify the shift in x, y and z coordinates of the table (calibration validity) measured by the IR camera system. In this study, maximum deviation of ± 3 mm from the calibration coordinates was accepted.

(A)



(B)

Figure 9 (A) The six marker neon localizer box with cross hairs and the goggle used in this study (B) Calibration setup with fixed couch vertical position using lasers.

4.2 IMAGE ACQUISITION

The planning CT images of the patients were acquired using Biograph true point HD CT scanner (Siemens, Germany). The patients were immobilized on a breast board with both arms abducted above the head. The planning CT images were acquired with 3 mm slice thickness from level of second cervical vertebra till the adrenals with field of view of 700 mm (maximum FOV) and the standard thorax imaging parameters. For all the patents, two sets of planning CT images were acquired with the same setup, one during the normal breathing cycle (free breathing) and the other one during deep inspirational breath hold.

4.3 TRACKING OF RESPIRATORY CYCLE

After acquiring the images of the patient during free breathing, the respiratory cycle of the patient was tracked by placing the localizer box on the patient in the treatment setup position. Initially, the baseline respiratory cycle was recorded. Following this, the patient was instructed through audio system to hold the breath in deep inspiration for 15 to 20 seconds to record the respiratory phase in DIBH. Planning CT images were acquired after two to three successive trials done to verify the patient's ability to perform DIBH. The same acquisition parameter was used while acquiring the DIBH images.

4.4 TREATMENT PLANNING

The planning CT images were transferred to the Eclipse treatment planning system (TPS) (Varian Medical Systems, USA). The free breathing and deep inspiration breath hold CT image sets were named as CT FB and CT DIBH respectively. The target (chest-wall and supraclavicular region), OARs (ipsilateral lung, contralateral lung, heart, LAD and contralateral breast) and other organs such as esophagus, liver, thyroid and spine were delineated as per the RTOG contouring guidelines (Breast Cancer Atlas for Radiation Therapy Planning, Radiation Therapy Oncology Group). The single isocenter 3D conformal field in field (FiF) treatment plans were generated in the Eclipse TPS for both FB and DIBH images. Two conformal tangent beams for the chest wall and one direct anterior beam for supraclavicular region were added and the FiFs were created in the tangential fields. 6 MV and 15 MV photon beams were used for the chest wall and supraclavicular regions respectively. The standard fractionation regimen of 50 Gy in 25 fractions over a period of 5 weeks was used for all the patients in this study.

PLAN EVALUATION PARAMETERS

S. No	Structures	Dosimetric Parameters	Cumulative DVH Mode
1	Target (CTV plus SC)	V95%, V105%, V107%, D98%, D2%, D_{min}, D_{max} and D_{mean} (Dose –Volume coverage)	Relative
2	Target (CTV plus SC)	HI and CI (Plan Quality Paramaters)	Relative
3	Ipsilateral Lung	V5 Gy, V20 Gy, V30 Gy and D_{mean}	Absolute
4	Combined Lung	V5 Gy, V20 Gy, V30 Gy and D_{mean}	Absolute
5	Contralateral Lung	V5 Gy and D_{mean}	Absolute
6	Heart	V5 Gy, V25 Gy, V30 Gy and D_{mean}	Absolute
7	LAD	V5 Gy, V10 Gy, V25 Gy D_{mean}	Absolute
8	Contralateral Breast	V5 Gy and D_{mean}	Absolute

4.5 DOSIMETRIC EVALUATION

I. TARGET

All the plans were evaluated by analyzing the dose distribution and dose volume histogram (DVH). For target volumes (CW and SC), the dosimetric parameters such as V95, V105, V107, D_{mean} and D_{max} were obtained from the cumulative DVH and the comparison was made between the DVH of the FB and DIBH plans using Eclipse TPS.

where, the parameters,

V95 corresponds to the volume of target receiving 95% of the prescription dose,

V105 corresponds to the volume of target receiving 105% of the prescription dose,

V107 corresponds to the volume of target receiving 107% of the prescription dose

D_{mean} and D_{max} are the mean and maximum dose received by the target volume respectively.

Additionally, the homogeneity and conformity indices (HI and CI) of the FB and DIBH plans were determined and compared. The homogeneity index was calculated by the following formula recommended by the international commission of radiation units and measures (ICRU report 83).

$$HI = D2 - D98 / D_{mean}$$

where,

D98 correspond to the absorbed dose received by 98% of target volume and

D2 correspond to the absorbed dose received by 2% of target volume

In ICRU report 83, the dosimetric parameters D_{min} and D_{max} are redefined as D98 and D2 which correspond to minimum and maximum absorbed dose or isodose received by the target volume respectively.

The CI was calculated by the following formula,

$$CI = VI / TV$$

where,

VI represents the volume of reference or prescription isodose in cc and

TV represents the volume of target in cc

II. OARs

A. IPSILATERAL LUNG AND COMBINED LUNG

For each patient, the V5, V20, V30 and D_{mean} of ipsilateral and combined lung volumes of the FB and DIBH treatment plans were analyzed and compared.

Where, the parameters,

V5 corresponds to the volume of lung receiving 5% of the prescription dose,

V20 corresponds to the volume of lung receiving 20% of the prescription dose, and

V30 corresponds to the volume of lung receiving 30% of the prescription dose.

B. CONTRALATERAL LUNG

For contralateral lung, the V5 and D_{mean} from cumulative DVH of FB and DIBH plans were analyzed and compared.

C. HEART

Of all the OARs, heart and the coronary vessels are the most important critical structures owing to the long term complications. For each patient, V5, V10, V25, V30, Dmean were analysed and compared.

Where,

V10 corresponds to the volume of heart receiving 10% of the prescription dose,

V25 corresponds to the volume of heart receiving 25% of the prescription dose,

V5 and D_{mean} as stated above.

D. LAD

The volume of LAD receiving 5 Gy, 10 Gy, 25 Gy and the mean doses (V5, V10, V25 and D_{mean}) were analyzed.

E. CONTRALATERAL BREAST

For contralateral breast volume, V5, D_{mean} and D_{max} of FB and DIBH plans were compared.

D_{max} corresponds to the maximum point dose received by the contralateral breast volume.

III. PLAN COMPARISON DVH

In addition, to the specific volume and dose comparison for the target and OARs, the plan comparison DVH which shows the entire isodose distribution of all the structures in the FB and DIBH treatment plans were analyzed for all the patients.

4.6 SAMPLE SIZE

Based on the data reported by Bruzzaniti et al (2013) the mean (range) of dose received by the lung in the deep inspirational breath hold was 4.64 (3.32-6.11), that is with the SD (standard deviation) of nearly 0.75 units (76). The same in the free breathing method was 5.51 (3.54-8.84), that is with the SD of nearly 1.25 units. In order to show the difference of nearly 0.9 unit that was statistically significant with alpha and beta errors at 5% and 20% respectively, the sample size needed was nearly 19 subjects (who will go through both methods).

4.7 STATISTICAL ANALYSIS

To compare the dosimetric parameters of the two samples (FB and DIBH) which can be paired with one another, the population mean (true mean of entire data) was used. Since our study involved comparison of two different planning techniques and same sets of measurements in the same subjects, a paired t-test statistical analysis was performed. (e.g. target coverage, Lung dose, heart dose and LAD doses determined from FB plan and DIBH plan with same treatment technique were compared).

Suppose a sample of n number of patients were planned on FB image sets, the same plan was then created in the DIBH images of the same patients to compare the dosimetric characteristics.

'x' is the dosimetric parameter determined from the FB plan

'y' is the dosimetric parameter determined from the DIBH plan

To study the null hypothesis that the actual mean difference is zero, the following steps are involved:

1. Calculate the actual difference between all the paired dosimetric parameters of FB and DIBH including positive and negative differences as stated below,

$$d_i = y_i - x_i$$

2. Calculate the mean difference, ***d'***

3. Calculate the standard deviation ***(SD)*** of ***d'***

4. Calculate the standard error ***(SE)*** of ***d'*** using following formula,

$$SE\ (d') = S_d / \sqrt{n}$$

5. Calculate the t-statistics,

$$T = d' / SE\ (d')$$

This statistic follows a t-distribution with n − 1 degrees of freedom under the null hypothesis

6. From the tables of t-distribution we compare our values for '**T'** to the $\mathbf{t_n - 1}$ distribution.

7. The above distribution gives the p-value (statistical significance) from the paired **t-test**.

5. RESULTS

In our study, single isocenteric Field in Field (FiF) forward IMRT conformal radiotherapy plans were generated using Eclipse TPS and the dosimetric parameters stated in the methodology (chapter 4) for target and OARs were analyzed.

5.1 PATIENT CHARACTERISTICS

In this study 19 patients were recruited and underwent the CT scan as per the study protocol, the mean age being 50 years (ranging from 33 to 72). Ten out of the nineteen patients had a BMI of more than 25 and the mean BMI was found to be 26 (ranging from 17.29 to 34.29). The patients were arbitrarily categorized into three age groups <40 years, 41 to 55 years and > 55 years to look for correlation between age and performance capacity in general. However, they were not categorised while comparing the dosimetric parameters in statistical analysis used in the study. Table 4 shows the detailed characteristics of the patients in our study.

Table 4 Patient characteristics

Patient ID	Hospital Number	Age	Weight (kg)	Height (cm)	BMI
1	794671F	54	47	157	19.07
2	844289F	36	52	146	24.39
3	615537C	48	69	153	29.48
4	875065F	59	59	145	28.06
5	849801F	39	79	170	27.34
6	854345F	49	70	154	29.52
7	868196F	33	65	155	27.06
8	011036G	37	66	158	26.44
9	004575G	63	60	164	22.31
10	038702G	58	76	167	27.25
11	150863G	72	62	159	24.52
12	160167G	41	90	162	34.29
13	089274G	58	63	156	25.89
14	035895G	60	52	143	25.43
15	267728G	38	60	156	24.65
16	228914G	43	62	165	22.77
17	142674G	47	62	160	24.22
18	140744G	44	41	154	17.29
19	163301G	62	62	155	25.81
	Mean	**50**	**63**	**157**	**26**
	Minimum	**33**	**41**	**143**	**17.29**
	Maximum	**72**	**90**	**170**	**34.29**

5.2 LUNG VOLUMES (Table 5&6)

The Primary aim of DIBH is to increase the volume of lung and to move the heart away from the chest wall. In our study, we evaluated the difference in lung volumes in three age groups and among individual patients. The minimum, maximum and mean difference in lung volumes (both ipsilateral and combined lung) averaged over each age group is listed in table 5. Though the patients in the age group <40 years showed considerable difference compared to other two groups in this study, it was not statistically significant. The lower values observed in the age group of 41 to 55 is due to one patient who could not perform the technique and th difference of only 40.24 cc was recorded overall for that patient.. Figure 10 (A) and (B) shows the patient image with poor and good performance during the study. The absolute volume of lung (combined and ipsilateral) measured for all the patients listed in table 6. There was a significant difference in the absolute volume of combined and ipsilateral lung obtained with FB and DIBH.

Table 5 The difference in lung volumes in FB and DIBH

Age category	Combined Lung (cc)			Ipsilateral Lung (cc)		
	Min	Max	Mean	Min	Max	Mean
< 40	1051.2	2177.3	1713.1	709.08	1007.3	874.02
41 to 55	40.24	1916.7	1285.1	15.11	904.66	621.95
> 55	775.49	2196.0	1561.2	319.43	1041.2	744.21

Table 6 Absolute volume of lung in FB and DIBH

Patient ID	Combined Lung volume (cc)			Left Lung Volume (cc)		
	FB	DIBH	Difference	FB	DIBH	Difference
1	1915.7	3644.4	1728.7	974.2	1867.3	893.1
2	1803.1	3736.6	1933.6	853.5	1751.3	897.8
3	1880.6	4057.9	2177.3	903.0	1910.3	1007.3
4	1718.1	3392.8	1674.7	774.3	1637.1	862.8
5	2642.0	3693.2	1051.2	1203.0	1912.0	709.1
6	2047.6	3713.5	1665.9	1015.0	1859.3	844.3
7	2175.4	3884.9	1709.5	988.1	1814.9	826.8
8	2312.2	3700.5	1388.3	1004.4	1685.8	681.4
9	2283.2	3246.2	963.1	1128.1	1584.6	456.6
10	**2718.3**	**2758.6**	**40.2**	**1146.8**	**1161.9**	**15.1**
11	1707.8	3020.0	1312.2	752.3	1377.0	624.7
12	1797.3	3714.0	1916.7	837.6	1742.3	904.7
13	1868.7	3556.9	1688.2	835.3	1695.8	860.5
14	2166.8	3693.4	1526.7	903.1	1641.8	738.7
15	2061.8	3261.6	1199.8	919.8	1524.9	605.1
16	1357.5	2133.0	775.5	516.3	835.8	319.4
17	1736.5	3252.9	1516.4	808.2	1518.6	710.4
18	1924.2	3950.3	2026.1	910.3	1844.6	934.3
19	1725.5	3921.5	2196.0	724.7	1765.8	1041.2

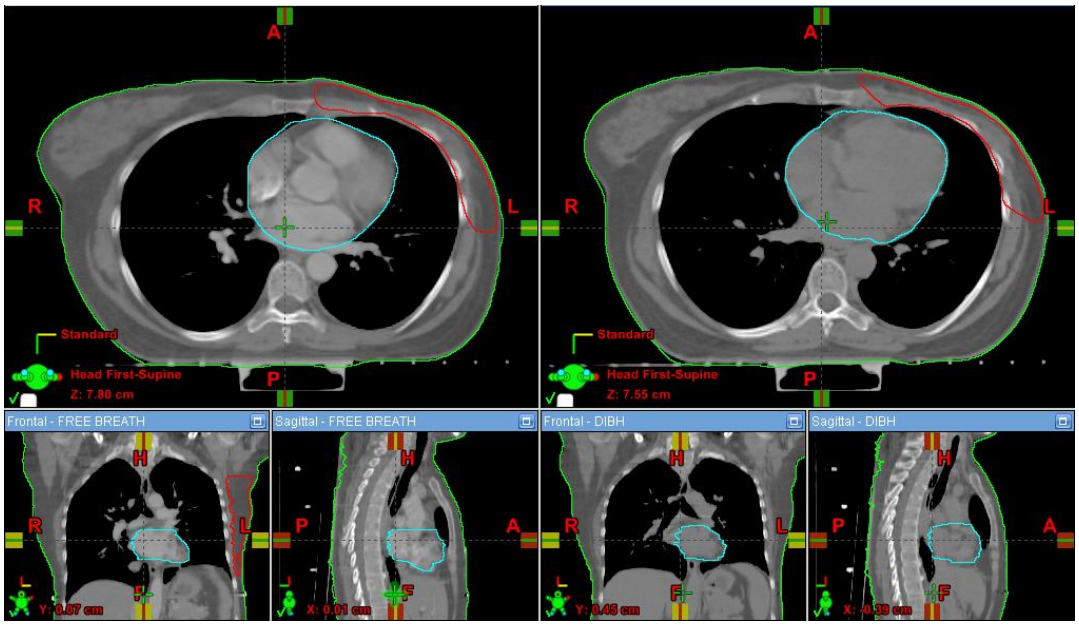


Figure 10 (A) CT image in FB and DIBH (all view) of the patient ID 10 (poor performance)

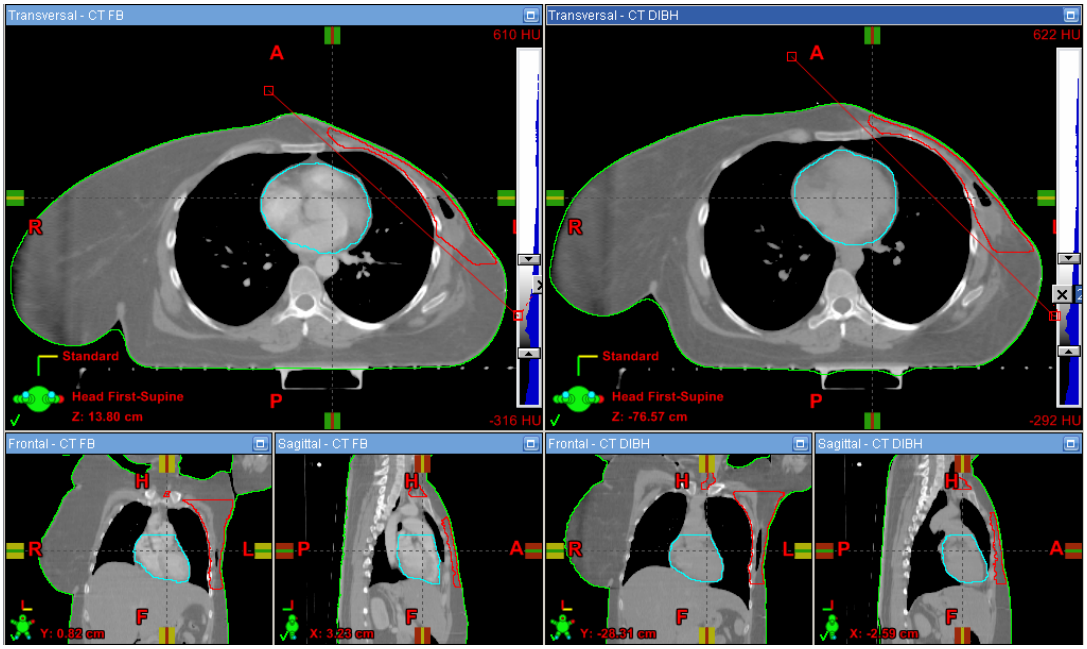


Figure 10 (B) CT images of the patient with good performance

5.3 DISTANCE OF HEART TO CHEST WALL (Table 7 & 8)

Based on the age groups, the mean distance between the heart and CW was analysed at two different levels, one at the centre of the heart in FB (taken as reference in this study) to centre of the heart in DIBH and the other plane in the DIBH image corresponding to the heart in FB Figure 11 shows the location of heart at the reference plane in FB and corresponding plane on DIBH.

The mean distances of heart from the CW are demonstrated in figure 12. Table 6 shows the minimum, maximum and mean heart distance observed in the specified age groups. From this result, the mean difference in the distance of the heart from chest wall is considerable in the patients below 40 years and above 55 years, but no overall correlation has been observed between age of the patient and the mean distance. The lesser values observed in the age group of 41 to 55 years could be attributed to the poor performance of the individuals in this group.

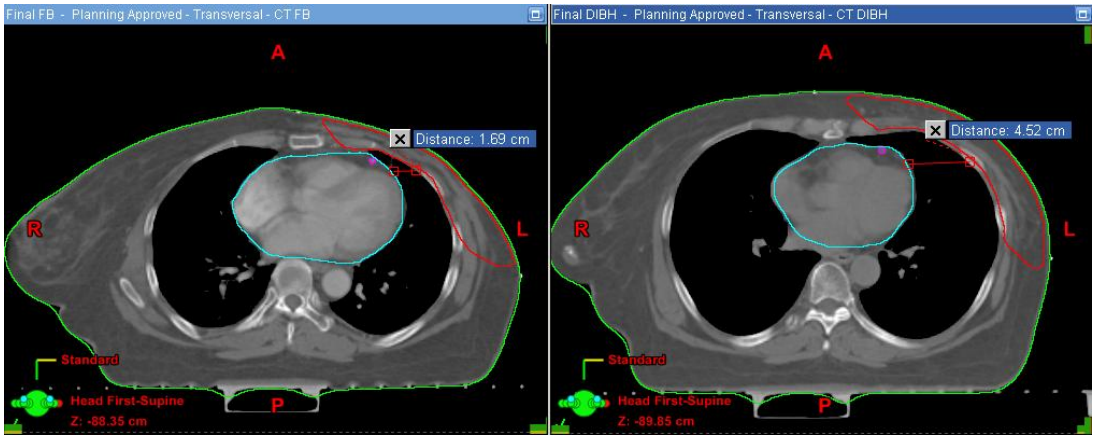


Figure 11 Location of heart at the reference plane in FB and corresponding plane on DIBH.

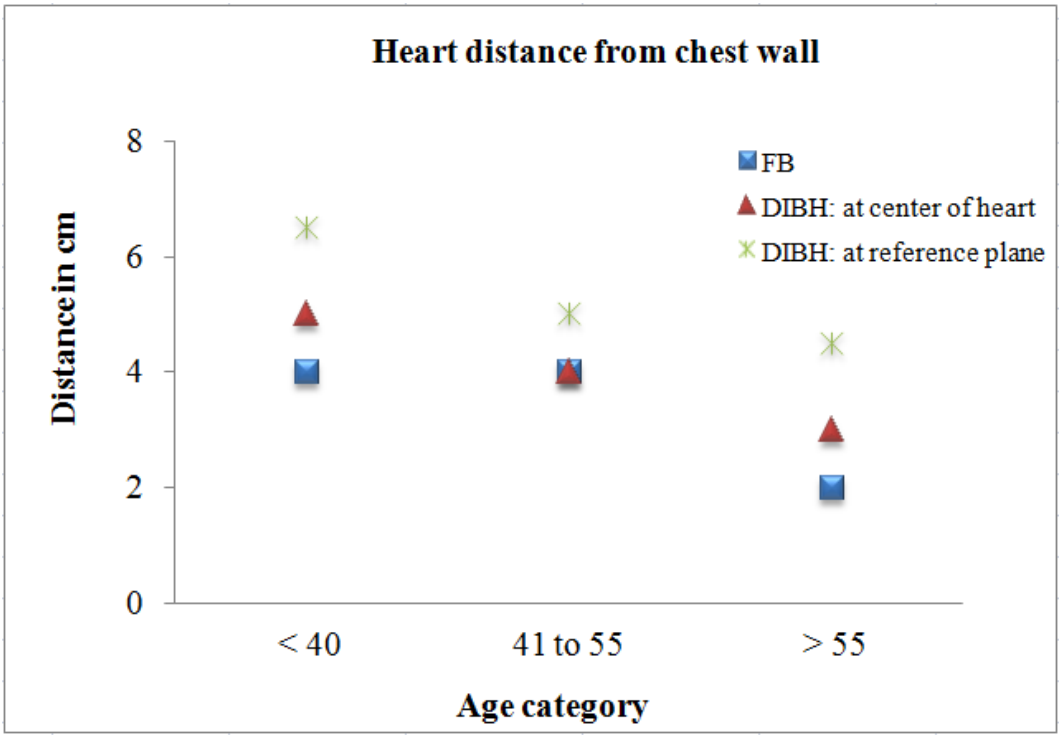


Figure 12 The mean heart distance from chest wall in FB and DIBH (at two planes)

Table 7 Distance between of heart to CW in DIBH (in the two planes) with respect to FB images

Age category	At center of heart (cm)			At reference plane (cm)		
	Min	Max	Mean	Min	Max	Mean
< 40	0.1	2	1.2	1.2	4	2.4
41 to 55	0	1.7	0.9	0.1	2.5	1.5
> 55	0.3	2.7	1.5	0.9	3.7	2.5

Table 8 Distance between of heart to CW in DIBH (in the two planes) with respect to FB images excluding the patient with poor performance

Age category	At center of heart (cm)			At reference plane (cm)		
	Min	Max	Mean	Min	Max	Mean
< 40	0.1	2	1.2	1.2	4	2.4
41 to 55	0.8	1.7	1.1	1.2	2.5	1.8
> 55	0.3	2.7	1.5	0.9	3.7	2.5

5.4 DOSIMETRIC ANALYSIS

Various dosimetric parameters were used in our study to compare the treatment plans generated in FB and DIBH images of the patients. For target volumes, V95, V105, V107 and D_{mean} were analyzed. Additionally,

the plan quality indices such as CI and HI were compared as stated above in the methods (chapter 4).

A. TARGET COVERAGE (Table 9)

In our study, dosimetrically comparable, single isocentered FiF forward IMRT plans were generated in FB and DIBH image sets and compared. Figure 13 shows the target coverage (95%) in three planes. Table 9 shows the dosimetric characteristics of FB and DIBH FiF plans. The target coverage is comparable which showed 97.8 ±0.9% and 98.1 ±0.8% (for V95) for FB FiF and DIBH FiF plan respectively. Further, the high dose regions V105, V107 and D_{mean} showed 6.1 ±3.4%, 0.2 ±0.3% and 101.9 ±0.5% for FB plans and 6.1 ±3.2%, 0.2 ±0.3% and 101.9 ±0.4% for DIBH plans respectively. Hence both the plans were dosimetrically identical with target coverage. The p – values were also found to be insignificant for all the parameters used. The same is illustrated in figure 14 which shows the plan comparison (PlanComp) DVH of FB and DIBH plans of one of the study patients. In addition, the plan quality indices such as CI and HI in FB plans were found to be 1.3 ±0.2 and 0.1 while 1.2 ±0.3 and 0.1 were recorded in DIBH plans. This substantiates the similarity of treatment plans computed both in FB and DIBH. Figure 11 and 12 shows the variation in CI and HI between FB and DIBH plans respectively.

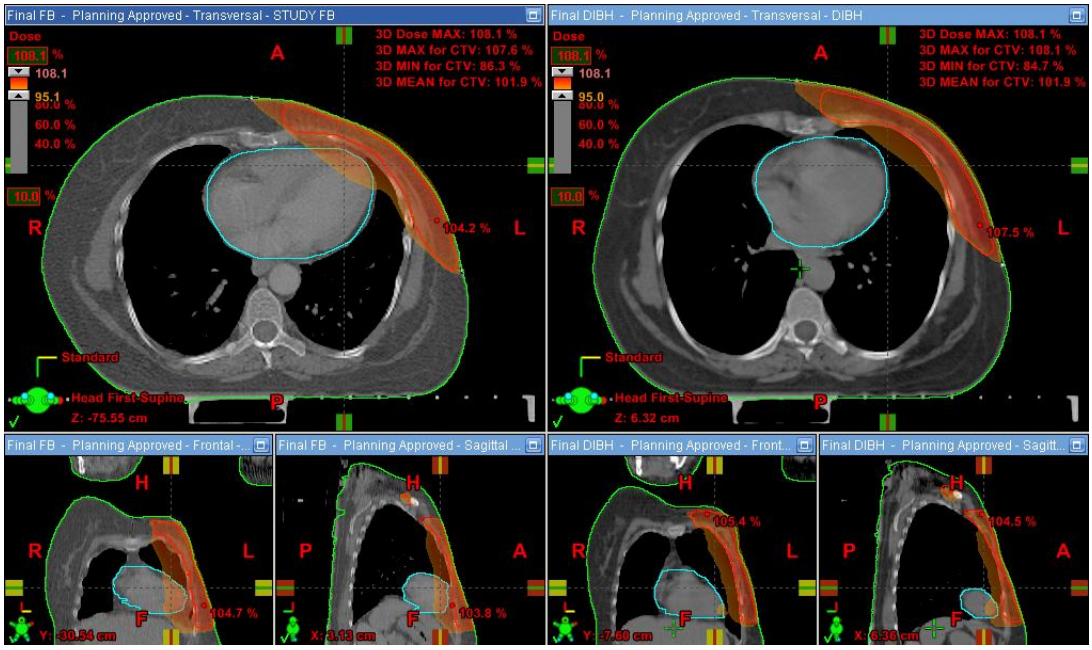


Figure 13 Identical target coverage (95%) in FB (left) and DIBH (right) in three planes

Table 9 Dosimetric characteristics of target volumes

Parameter	FB (%)				DIBH (%)				P-Value
	Min	Max	Mean	SD	Min	Max	Mean	SD	
V95	96.1	99.1	97.8	0.9	96.3	99.1	98.1	0.8	0.150
V105	0.4	11.8	6.1	3.4	0.2	11.1	6.1	3.2	1.000
V107	0.0	0.9	0.2	0.3	0.0	0.9	0.2	0.3	0.950
Dmean	100.9	102.8	101.9	0.5	101.1	102.5	101.9	0.4	0.950
CI	1.0	1.9	1.3	0.2	0.9	2.2	1.2	0.3	0.238
HI	0.1	0.0	0.1	0.0	0.1	0.0	0.1	0.0	0.523

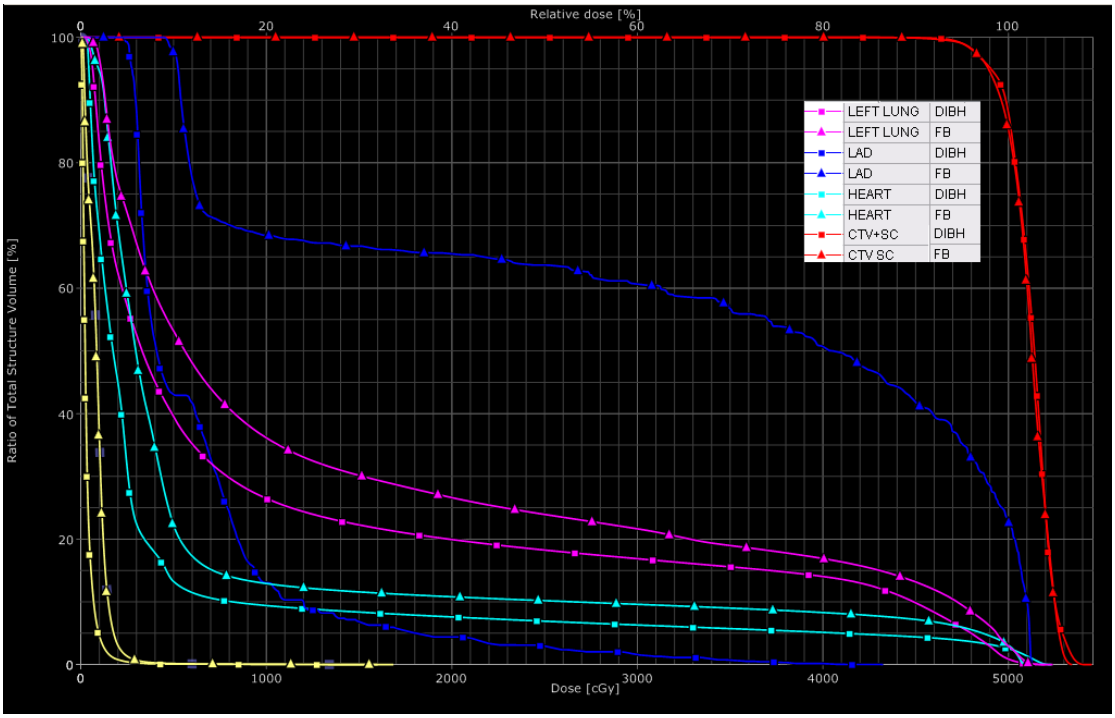


Figure 14 PlanComp DVH of FB (triangle) and DIBH (square)

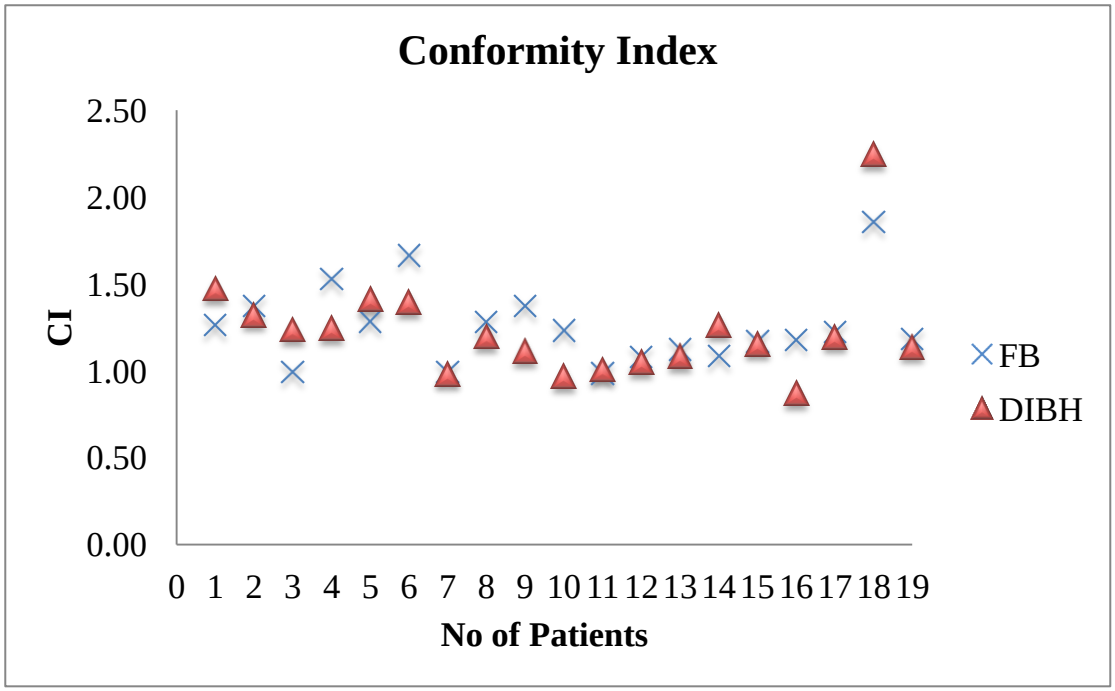


Figure 15 Differences in CI between FB and DIBH

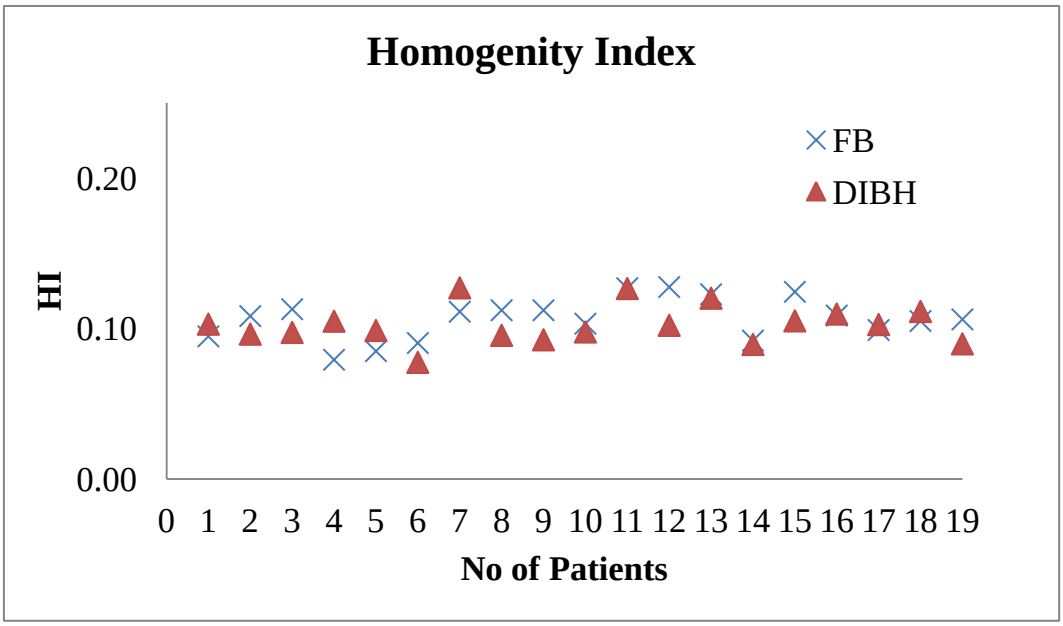


Figure 16 Differences in HI between FB and DIBH

B. LUNG DOSES (Table 10, 11 & 12)

The lung volumes (Ipsilateral, Contralateral and Combined) were analyzed separately with various dose volume parameters.

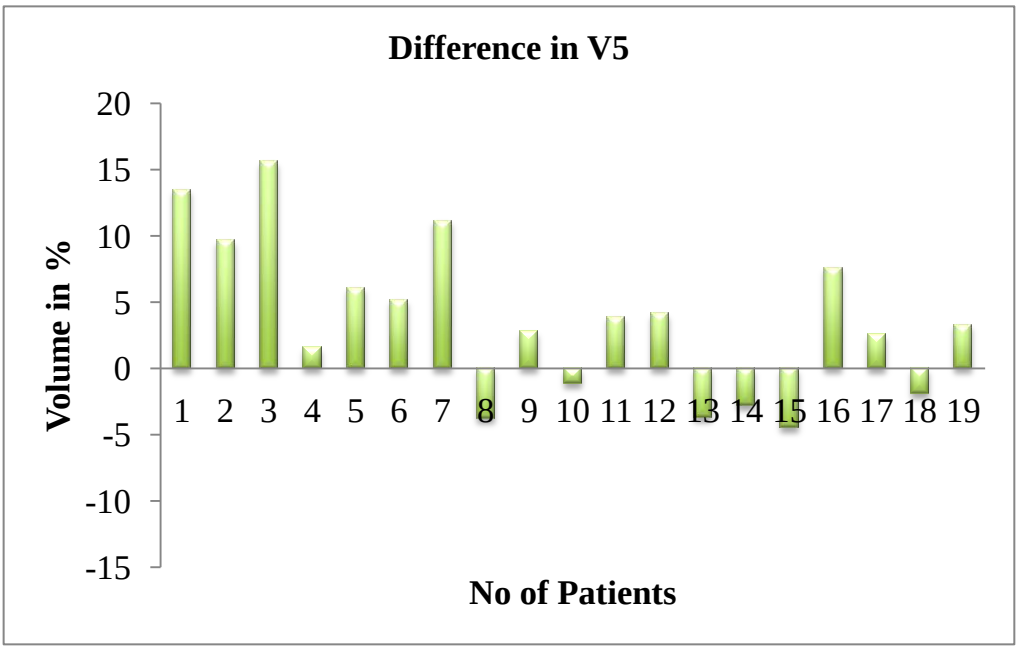
I. IPSILATERAL LUNG (Table 10)

The ipsilateral lung volumes were analysed using four different dose volume parameters such as V5, V20, V30 and D_{mean}, among which the V20 and Dmean are widely used to estimate the radiation induced side effects (77,78). Table 10 shows the mean dosimetric characteristics of ipsilateral lung for the above parameters. The differences in V5, V20, V30 and Dmean are illustrated in figure 17.

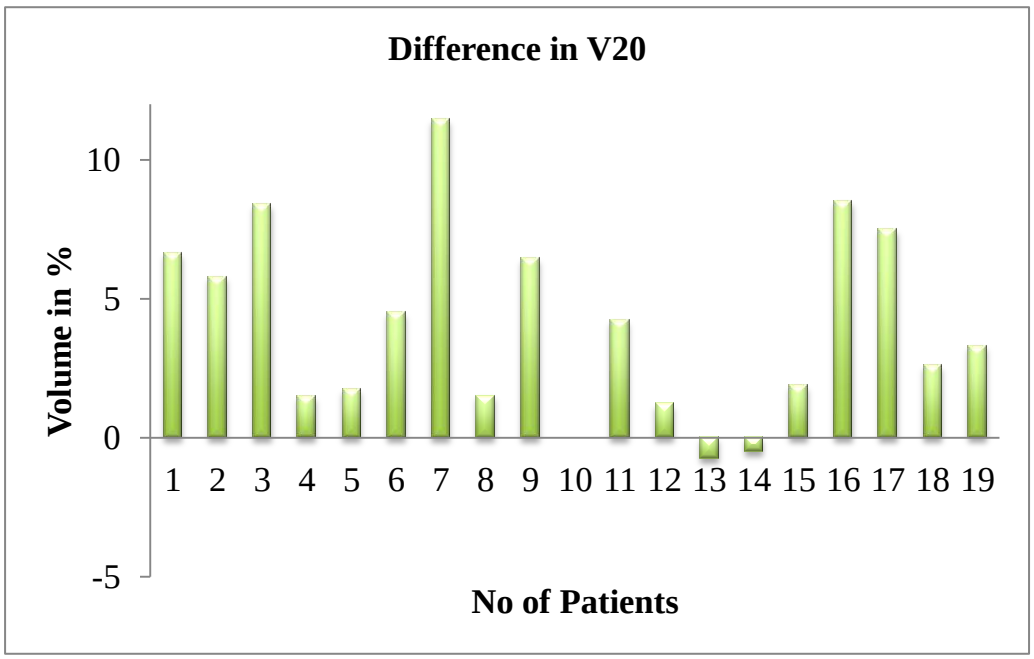
Though, the mean V5 of ipsilateral lung showed only a small difference in DIBH with respect to FB, it was found to be statistically significant (p value of 0.015). Similarly, the V20 and V 30 along with Dmean were also found to be statistically significant (p values of 0.003).

Table 10 Dosimetric characteristics of ipsilateral lung volume

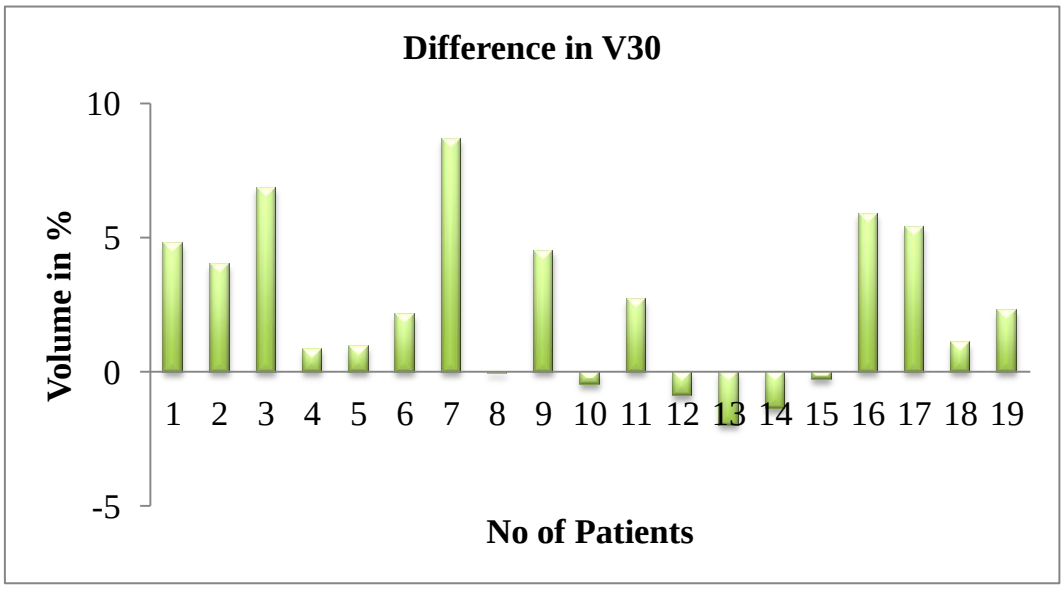
Parameter	FB (%)				DIBH (%)				P-Value
	Min	Max	Mean	SD	Min	Max	Mean	SD	
V5	38.01	56.73	48.82	6.17	34.99	54.2	45.18	5.69	0.015
V20	16.39	32.21	25.44	4.32	15.97	27.7	21.45	3.42	0.003
V30	11.02	25.7	20.09	3.75	12.4	22.3	17.72	3.07	0.003
Dmean	9.42	16.42	13.59	2.05	9.07	15.3	12.13	1.73	-



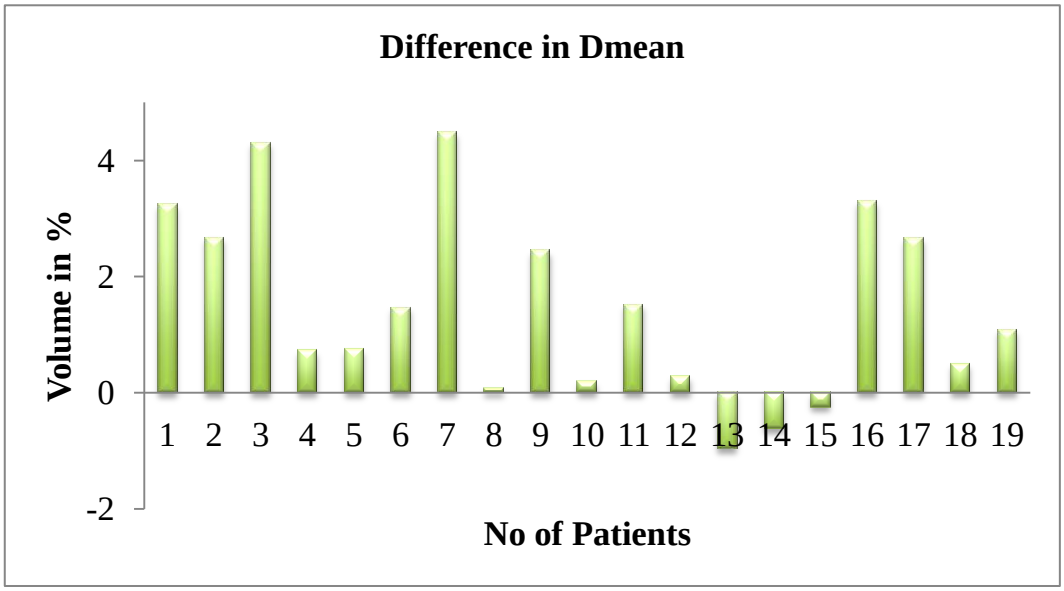
(A)


Difference in V20
Volume in %
10
5
0
-5
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
No of Patients

(B)


Difference in V30
Volume in %
10
5
0
-5
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
No of Patients

(C)



(D)

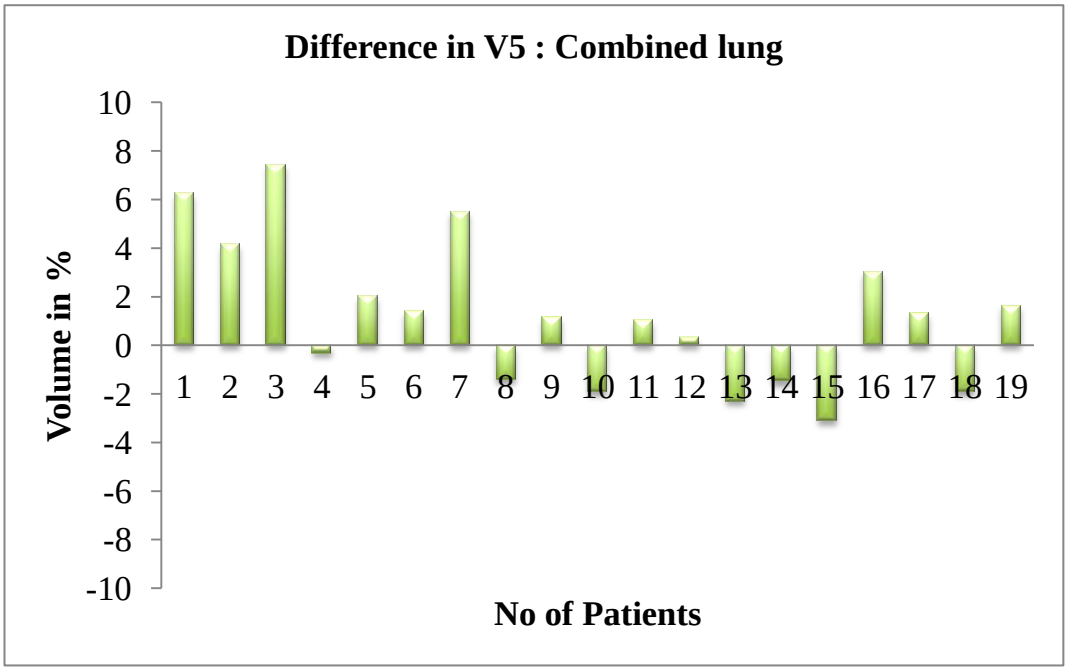
Figure 17 Difference in doses received by ipsilateral lung in FB and DIBH (A) V5 (B) V20 (C) V30 (D) D_{mean}

II. COMBINED LUNG (Table 11)

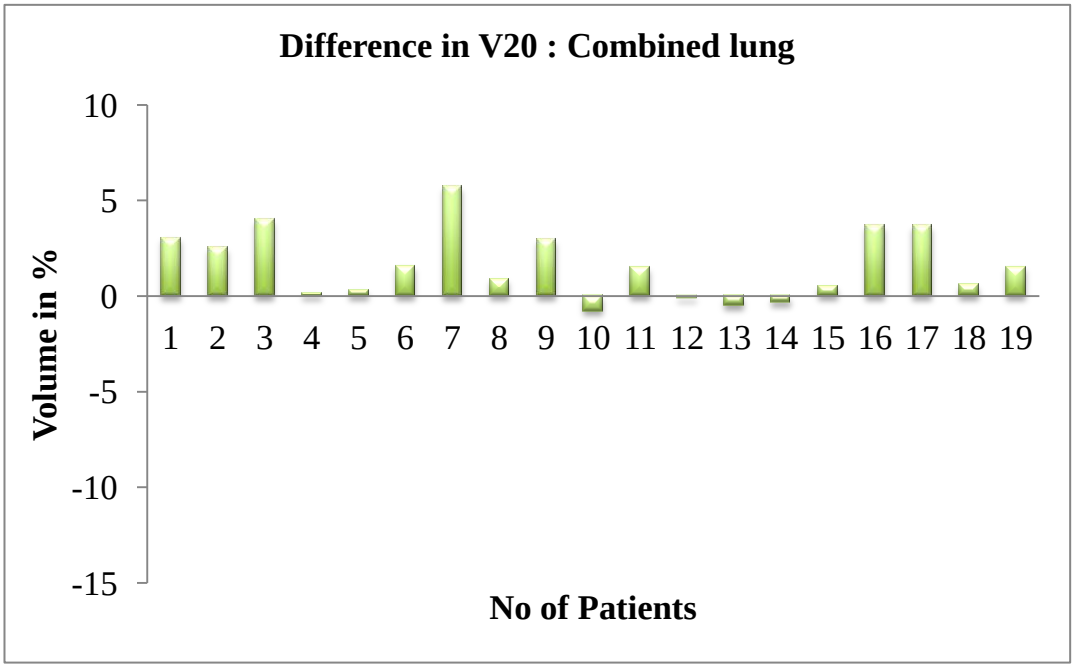
Similarly, for combined lung, the same dosimetric parameters were used and reported in table 11. Since, combined lung includes the contralateral lung which is not involved in tangential FiF technique, the dosimetric parameters were found to be similar with no significant difference.

Table 11 Dosimetric characteristics of combined lung volume

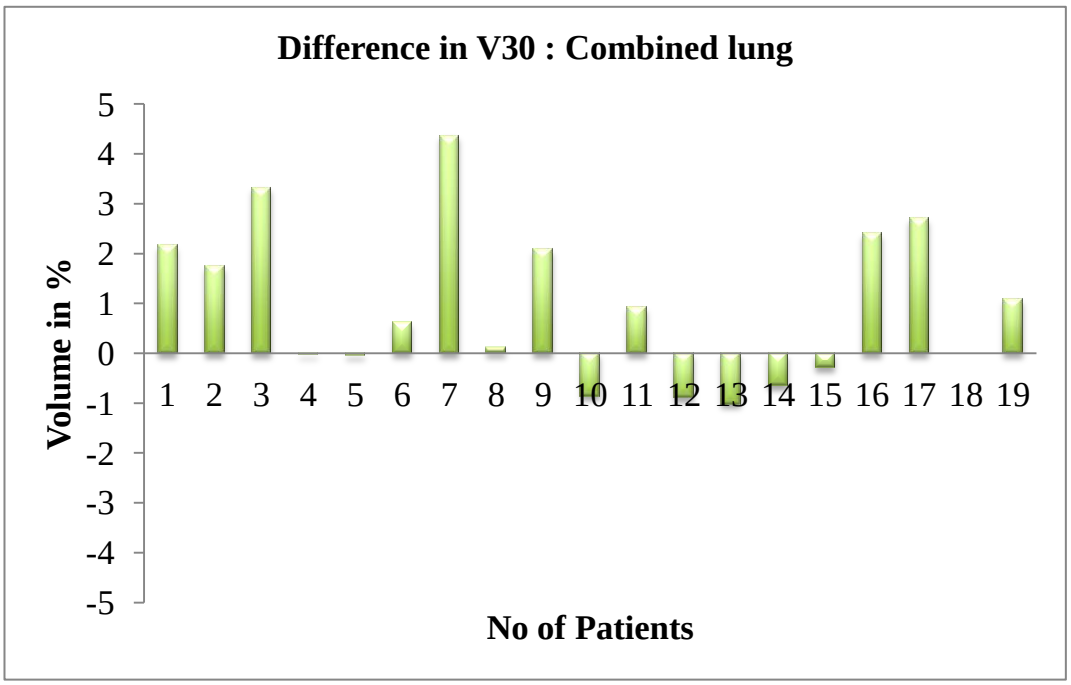
Parameter	FB (%)				DIBH (%)				P-Value
	Min	Max	Mean	SD	Min	Max	Mean	SD	
V5	14.6	26.5	22.26	3.44	15.55	25.2	21.07	3.13	0.100
V20	6.27	15.5	11.62	2.36	6.6	12.6	10.73	1.78	0.340
V30	4.2	12.6	9.18	2.02	4.85	10.5	8.25	1.129	0.018
Dmean	4.1	8.19	6.49	1.12	4.38	7.2	5.91	0.908	0.011



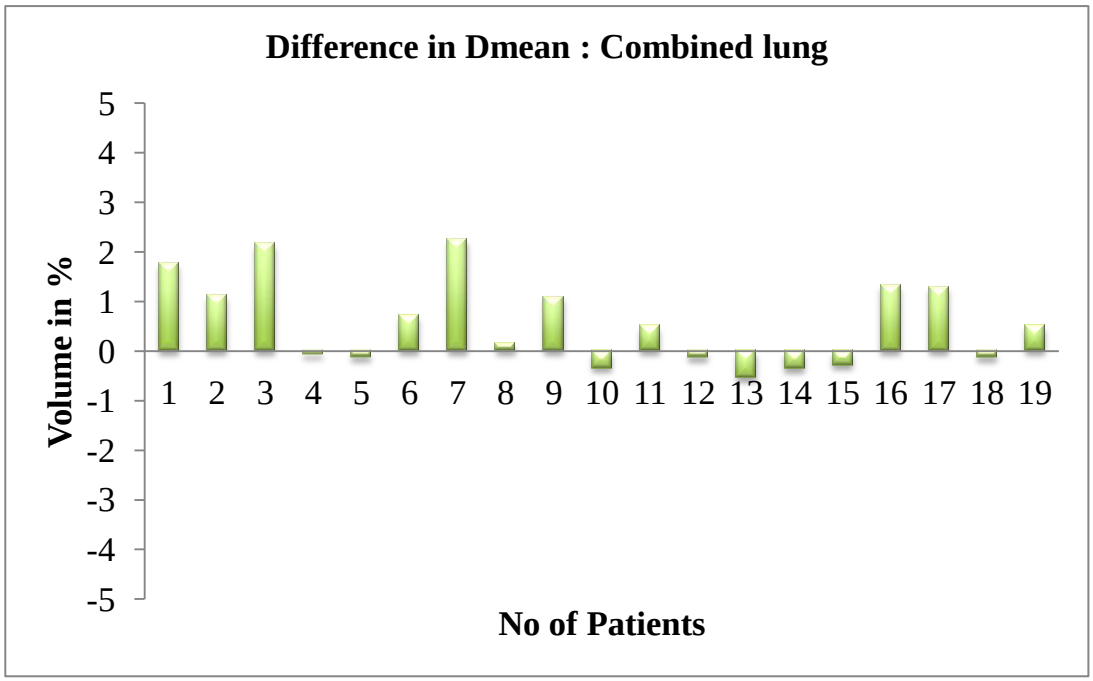
(A)


Difference in V20 : Combined lung
10
5
0
-5
-10
-15
Volume in %
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
No of Patients

(B)


Difference in V30 : Combined lung
5
4
3
2
1
0
-1
-2
-3
-4
-5
Volume in %
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
No of Patients

(C)



(D)

Figure 18 Difference in doses received by combined lung in FB and DIBH (A) V5 (B) V20 (C) V30 (D) D_{mean}

III. CONTRALATERAL LUNG (Table 12)

As stated above, the contralateral lung is not involved in tangential FiF conformal treatment plan, the parameters V5 (represents low dose spread) and D_{mean} were analysed. Table 12 shows the dose volume report of contralateral lung. From above table, it is observed that the dosimetric characteristic of FiF plan which contributes very low doses to the contralateral lung volume. The p value (0.645) showed statistically insignificant difference between the FB and DIBH plans for D_{mean}. Majority of the patients in this study showed 0% volume for V5. Figure 19 shows the variation in V5 of contralateral lung.

Table 12 Dosimetric characteristics of contralateral lung volume

Parameter	FB (%)				DIBH (%)				P-Value
	Min	Max	Mean	SD	Min	Max	Mean	SD	
V5	0	0.18	0.025	0.56	0	0.4	0.06	0.11	0.011
Dmean	0.3	1.01	0.517	0.212	0.28	0.84	0.495	0.16	0.645

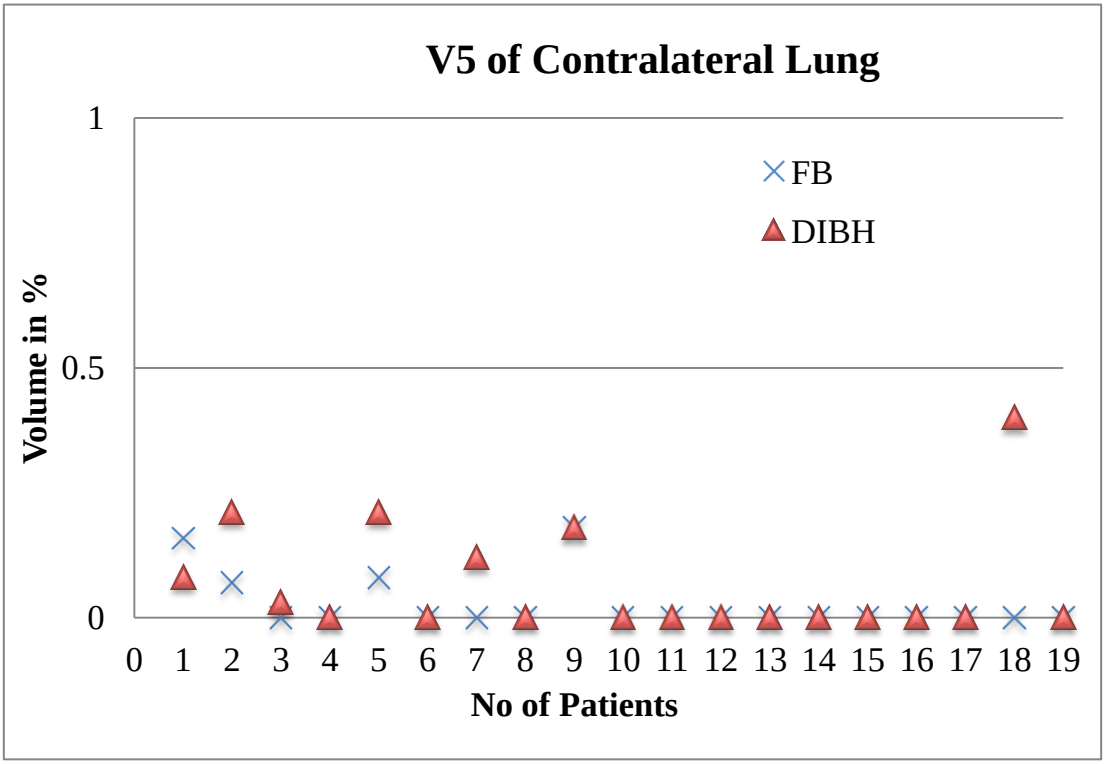


Figure 19 Variation in V5 of contralateral lung in FB and DIBH

C. HEART (Table 13)

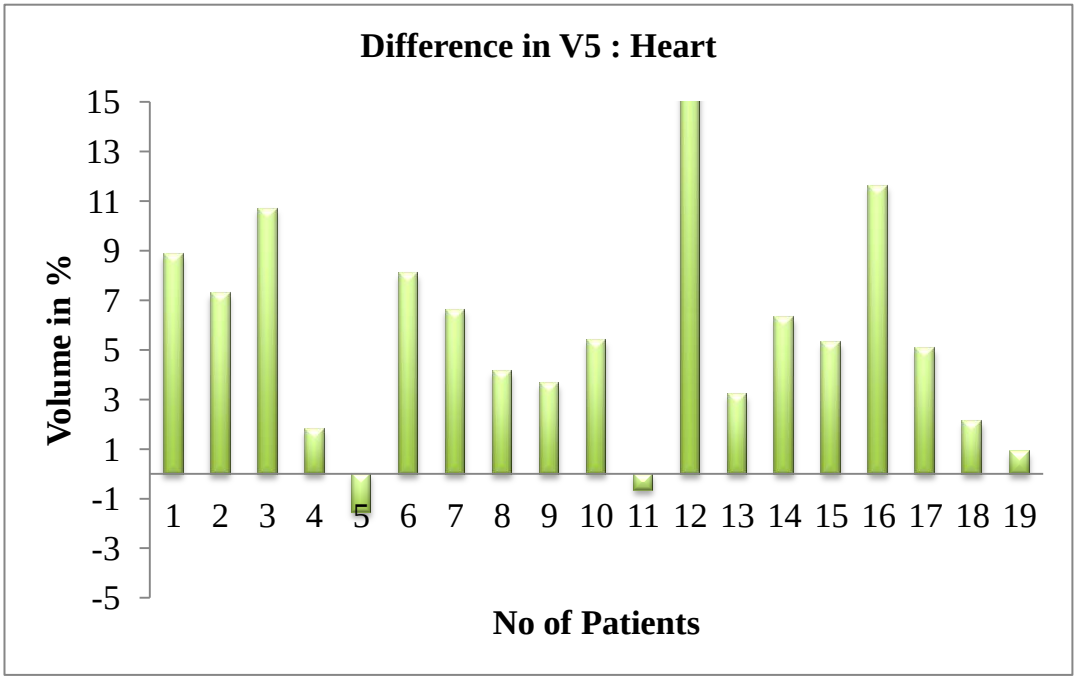
Heart is one of the main organs at risk while delivering radiotherapy to the thoracic region and more so during the treatment of left sided breast cancer patients accounting for the long term morbidity and mortality. In breast radiotherapy, the V25 and D_{mean} is most commonly used dose volume parameter for evaluating the breast radiotherapy plans. In our study, the FB and DIBH plans were evaluated using five different parameters namely, V5, V10, V25, V30 and D_{mean}. Where the V5 (5 Gy volume) corresponds to low dose spread to heart in percentage. For better dosimetric evaluation, two additional dose volume parameters V10 and V30 were used in our study. Table 13 shows the detailed report of the parameters analysed for heart in FB and DIBH plans. Figure 20 shows the difference in doses received by the heart for all the parameters studied.

Statistical analysis showed that there was significant reduction in dose to heart in the DIBH plans for all the parameters that were analysed as compared to FB plans (p value of nearly 0.0 for all the parameters). According to Quantitative Analysis of Normal Tissue Effects in the Clinic (QUANTEC), 2010, the tolerance for heart in conformal radiotherapy to breast is V25 $\leq$ 10% which represents 10% of the heart volume should not receive more than 25 Gy. It was observed that V25 of heart was 9.12 ±4.71% in FB FiF plan while the same was as 4.85 ±5.2% in DIBH plan, which reduced the V25 almost half with respect to FB plan.

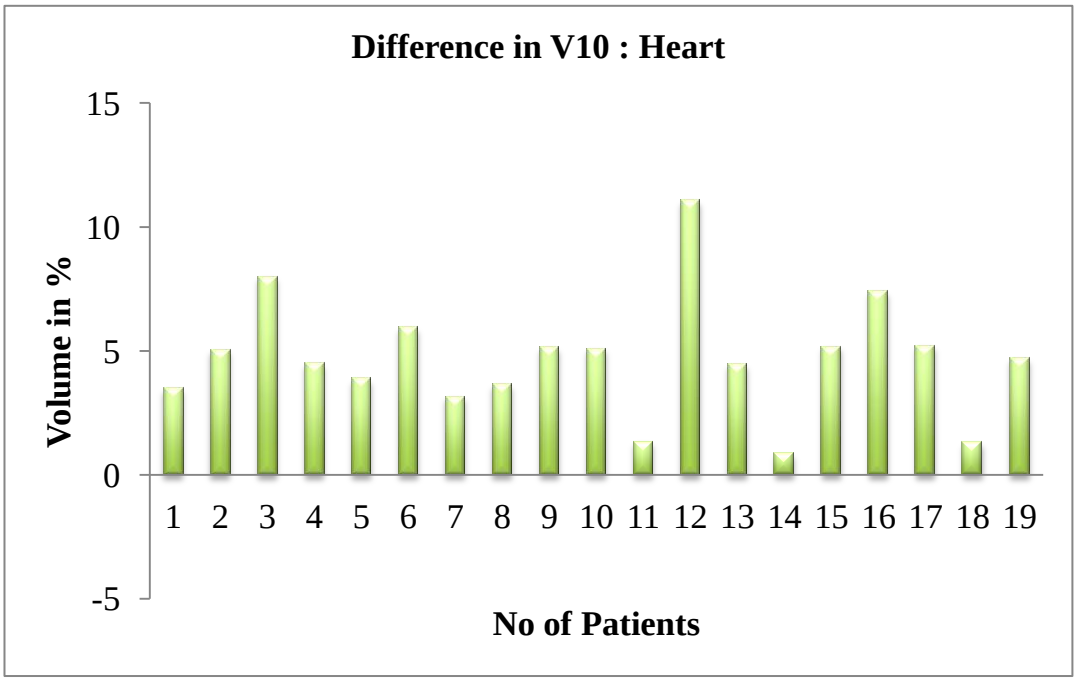
Similar results were also found for V30 where the heart volume in FB showed 8.43 ±4.48% while DIBH showed 4.71 ±4.57%. Other parameters: V5, V10 and D_{mean} also showed statistically significant results (p value of nearly 0.0) for heart volume which clearly supports the DIBH technique for left sided breast cancer patients to reduce the radiation induced side effects without compromising the target coverage.

Table 13 Dosimetric characteristics of Heart

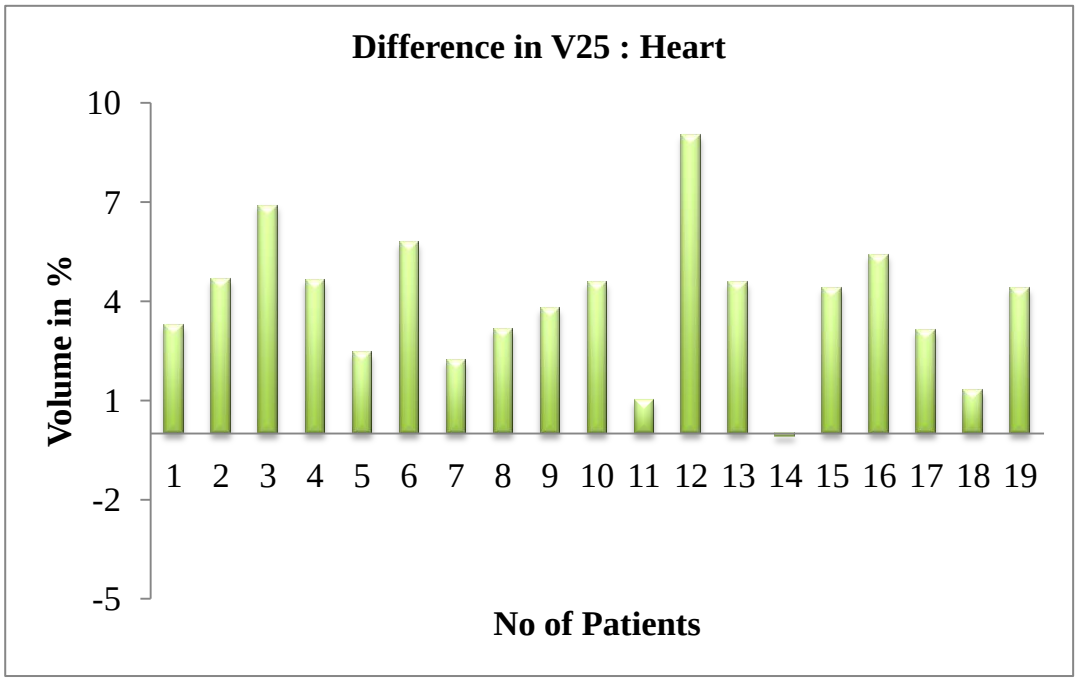
Parameter	FB (%)				DIBH (%)			
	Min	**Max**	**Mean**	**SD**	**Min**	**Max**	**Mean**	**SD**
V5	9.77	46.7	21.44	9.43	4.18	40.4	15.74	9.15
V10	4.43	24.15	12.42	5.65	0.5	23.3	7.72	5.98
V25	2.55	18.3	9.12	4.71	0	18.4	4.85	5.21
V30	2.22	17.2	8.43	4.48	0	17.4	4.71	4.57
Dmean	3.1	12.35	6.827	2.69	1.81	12.09	4.775	2.59


Difference in V5 : Heart
Volume in %
15
13
11
9
7
5
3
1
-1
-3
-5
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
No of Patients

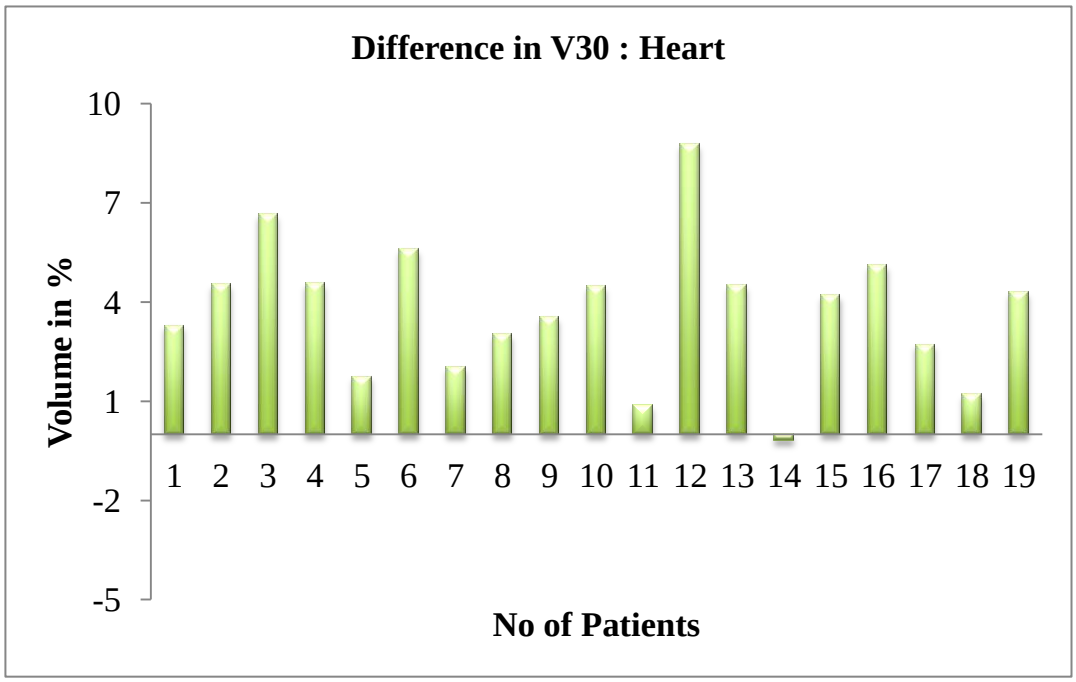
(A)


Difference in V10 : Heart
Volume in %
15
10
5
0
-5
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
No of Patients

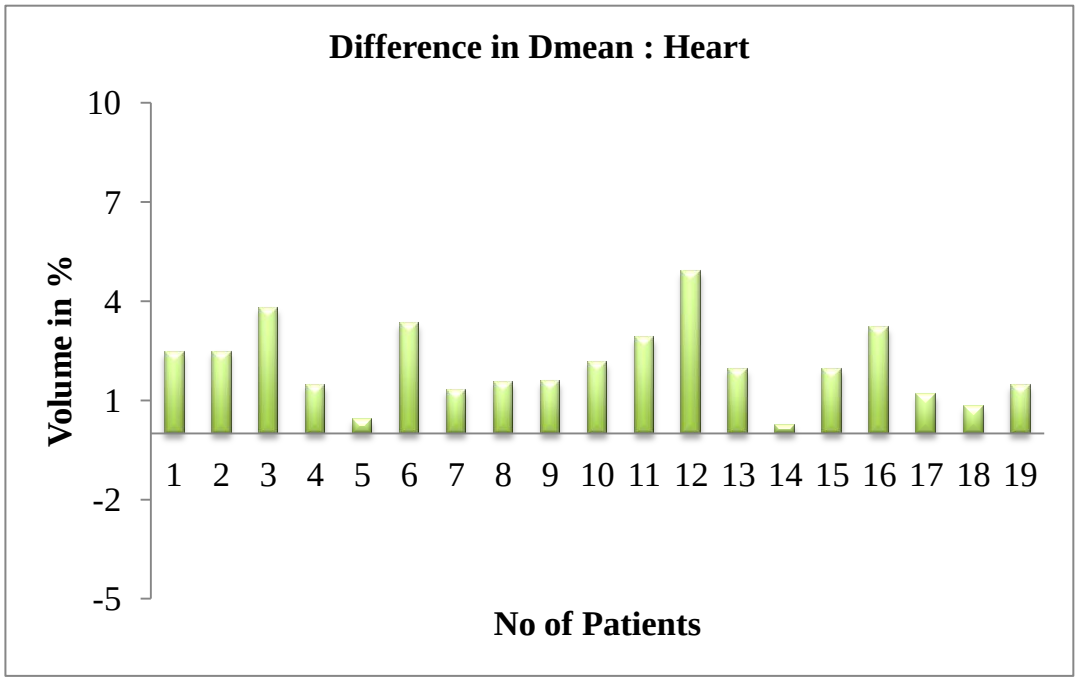
(B)


Difference in V25 : Heart
Volume in %
10
7
4
1
-2
-5
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
No of Patients

(C)


Difference in V30 : Heart
Volume in %
10
7
4
1
-2
-5
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
No of Patients

(D)



(E)

Figure 20 Difference in doses received by heart in FB and DIBH (A) V5 (B) V10 (C) V25 (D) V30 and (E) D_{mean}

D. LAD (Table 14)

LAD is involved while delivering radiation to the left chest wall as the dose is mostly received by the anterior part of the heart where it is located. Doses received by the LAD are directly proportional to the risk of development of radiation induced ischemic heart disease. Hence in our study, LAD doses were evaluated in the FB and DIBH plans with four different dose volume parameters (V5, V10, V25 and D_{mean}). Since the volume of LAD is only about 1 cc, delineating and evaluating LAD is a difficult task for the physician. Delineation of LAD in our study was restricted due to the slice thickness, motion artifacts and the wash out of contrast before taking the second set of CT images (DIBH). Table 14 shows the LAD dose observed from the FB and DIBH plans. As very few studies in the literature dealt with doses to the LAD and no standard protocols for estimation of LAD doses and limiting factors or tolerances were defined, the parameters used for estimating doses to the heart were used for LAD in our study. However, due to its location and considerable variations in its delineation according to the physicians expertise, V5 for LAD is unreliable and the standard deviation observed in the V5 is an evidence for the same. A significant reduction of about 50% in the doses to the LAD in DIBH plans was observed in our study in comparison with the FB plans. Further, in FB plans, there was lot of fluctuation in the doses to the LAD due to the respiratory motion which could be avoided in the DIBH plans. The color wash of 95% isodose at level LAD in same plane is illustrated in figure 21.

The dose difference between FB and DIBH for all the four parameters were significant and are illustrated in figure 22.

Table 14 Dosimetric Characteristic of LAD

Parameter	FB				DIBH				P-Value
	Min	Max	Mean	SD	Min	Max	Mean	SD	
V5	14.2	97.56	25.24	53.47	12.51	81.84	41.3	19.81	0.03
V10	0	86.5	39.52	24.61	0	50	19.94	15.43	0.002
V25	0	72.48	31.91	24.47	0	45	12.48	15.74	0.002
Dmean	4	36.94	17.84	10.73	3.06	23.16	9.66	6.454	0.001

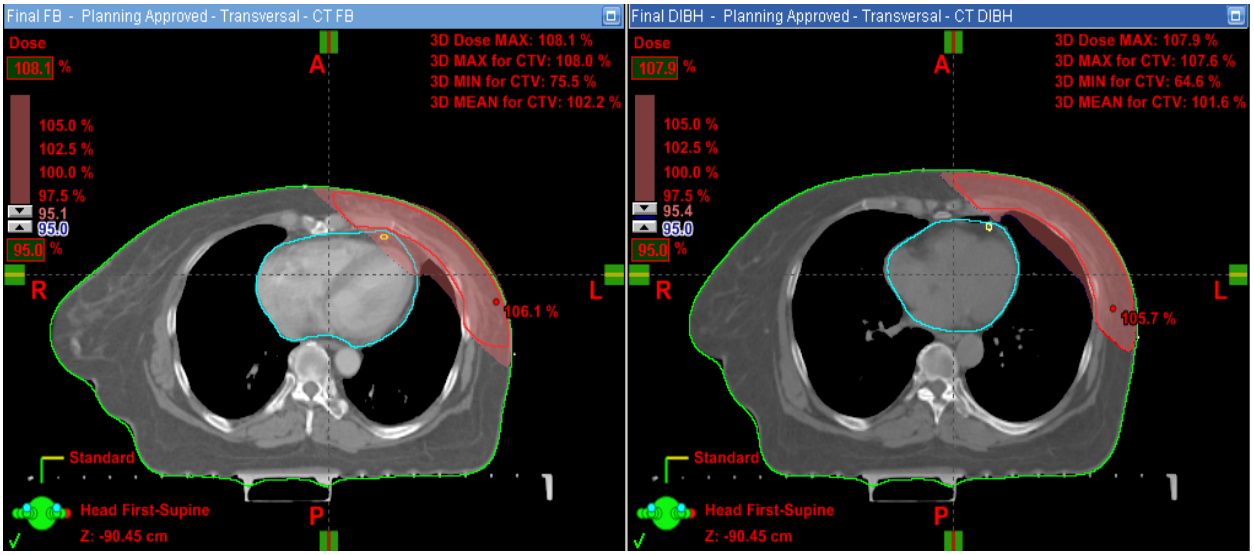
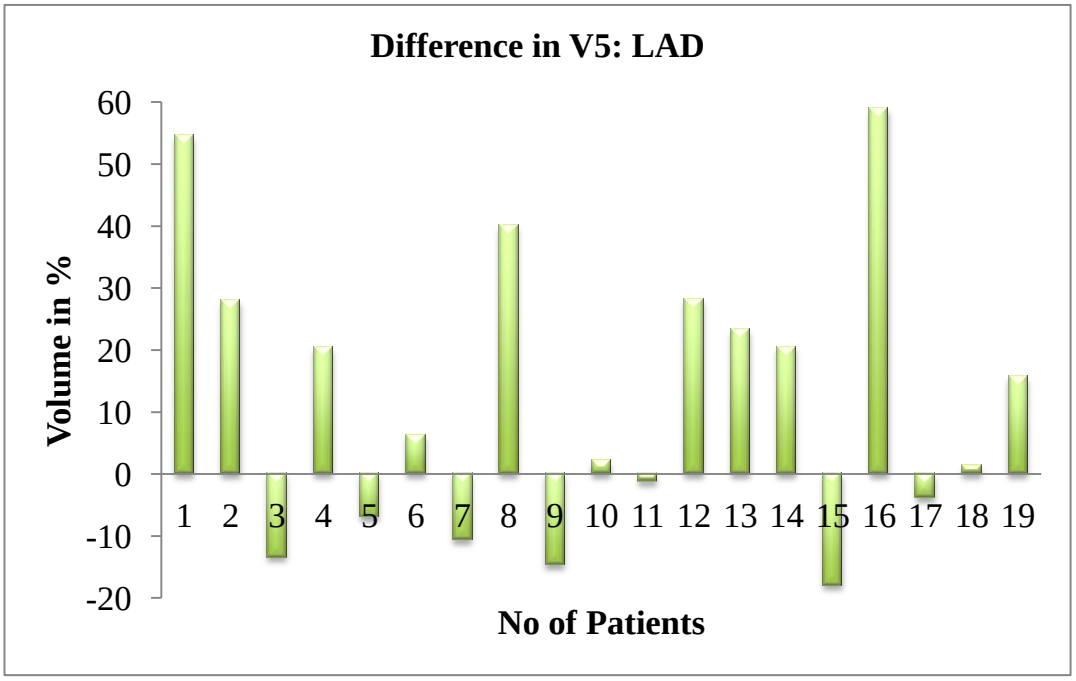
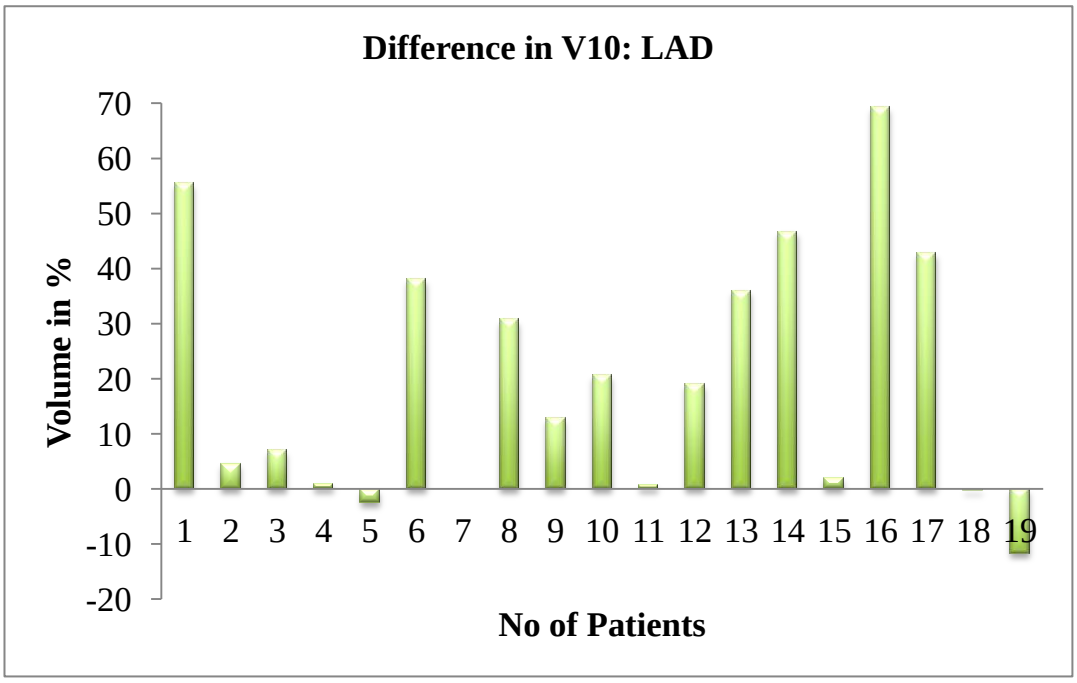


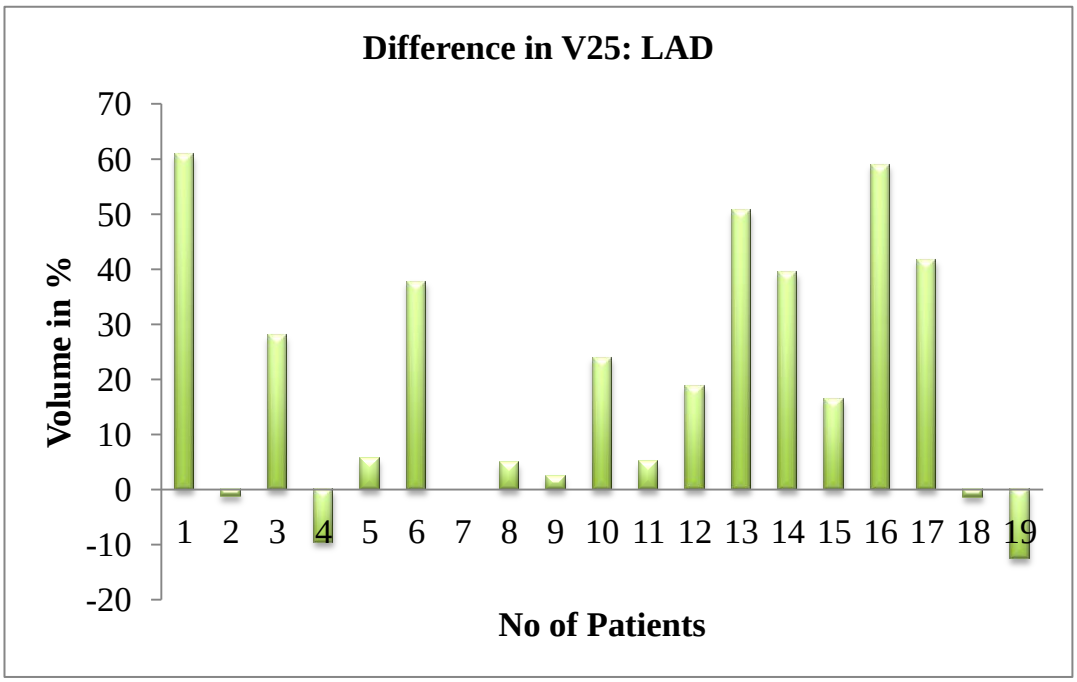
Figure 21 The color wash of 95% isodose at the level of LAD


Difference in V5: LAD
Volume in %
60
50
40
30
20
10
0
-10
-20
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
No of Patients

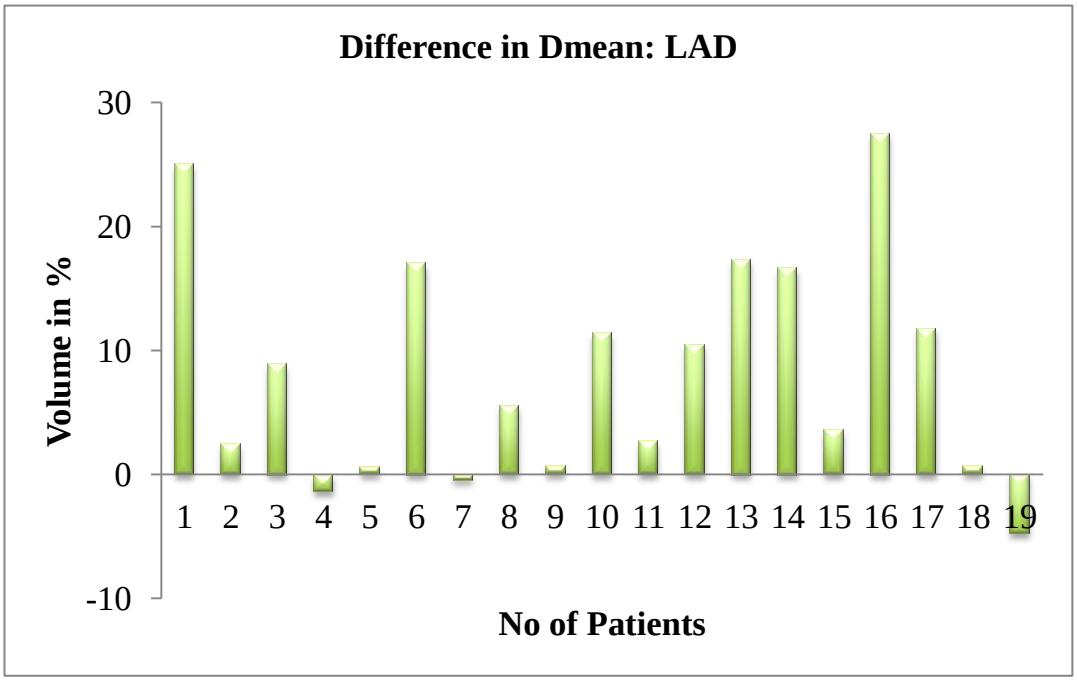
(A)


Difference in V10: LAD
Volume in %
70
60
50
40
30
20
10
0
-10
-20
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
No of Patients

(B)



(C)



(D)

Figure 22 Difference in doses received by LAD in FB and DIBH

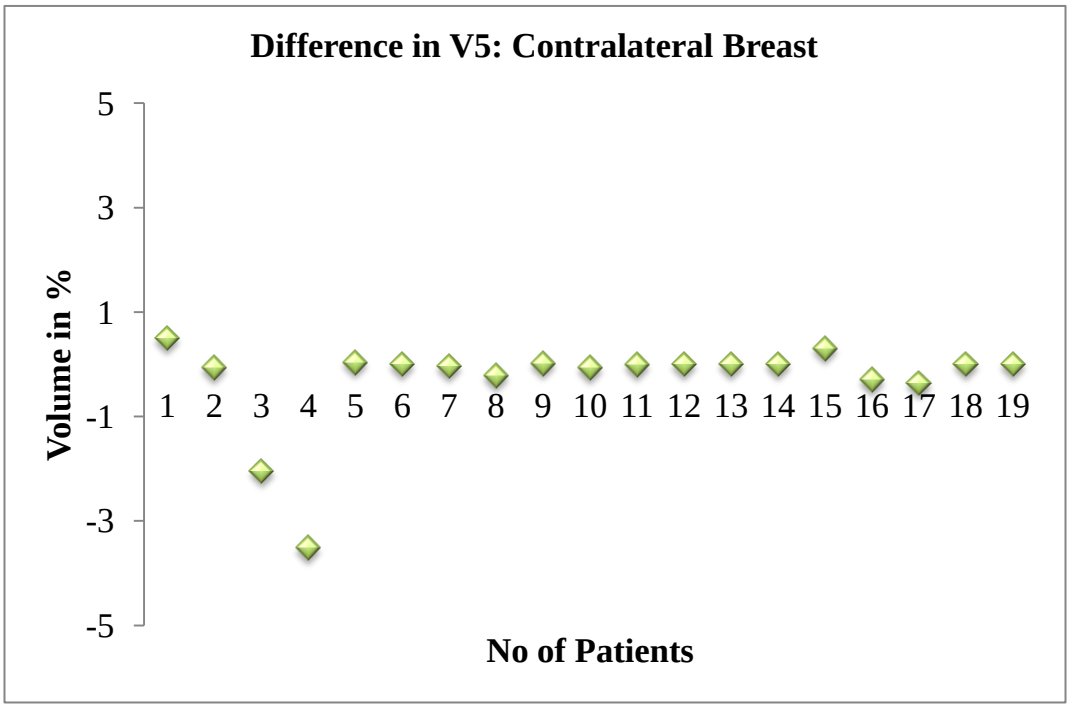
(A) V5 (B) V10 (C) V25 (D) D_{mean}

E. CONTRALATERAL BREAST

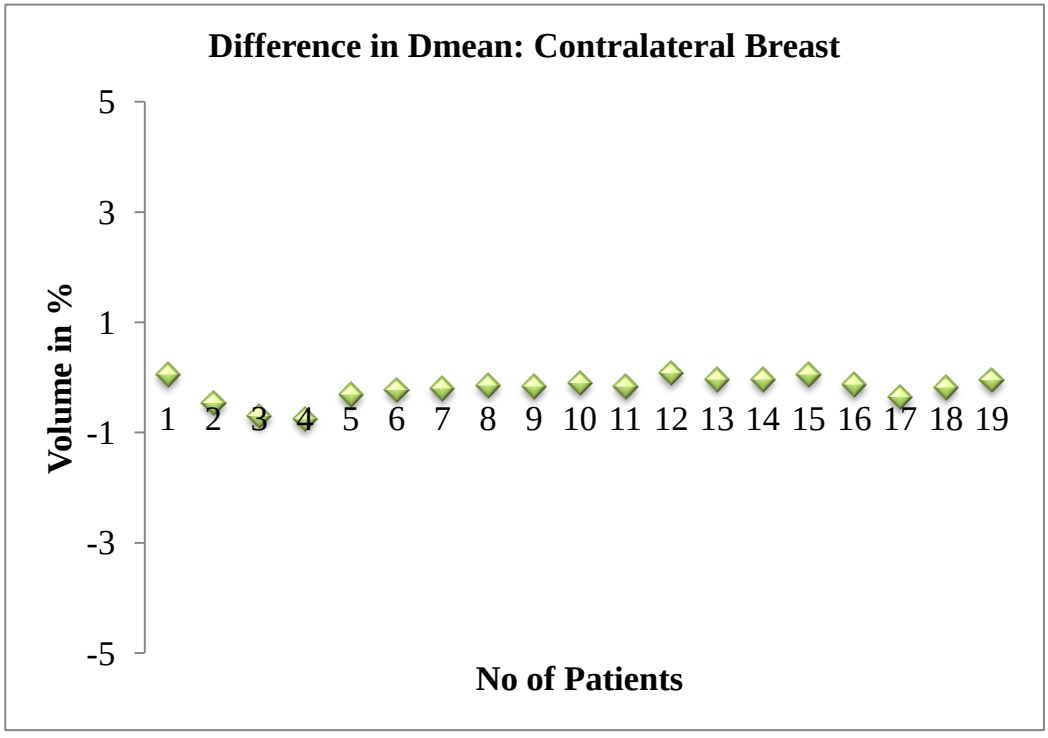
There is probability of development of second malignancy in the contralateral breast due to the scattered dose delivered to contralateral breast volume during radiotherapy for breast cancer. In our study, we have evaluated three different parameters for contralateral breast which accounts for the same. The dose volume characteristic of contralateral breast is listed in table 15. Since the dose is mainly contributed from the scattered dose, majority of the patients showed no difference in the doses received in FB and DIBH, as shown in figure 23.

Table 15 Dosimetric characteristics of contralateral breast

Parameter	FB				DIBH				P-Value
	Min	Max	Mean	SD	Min	Max	Mean		
V5	0	4.56	0.44	1.038	0	6.61	0.75	1.698	0.16
Dmax	3.47	47.59	20.26	10.96	3.46	47.7	18.83	12.35	0.39
Dmean	0.08	1.47	0.45	0.333	0.2	2.17	0.66	0.48	0.001



(A)



(B)

Figure 23 Difference in contralateral doses. V5 (A) and D_{mean} (B)

6 DISCUSSION

The advent of combined modality treatment approach in the management of breast cancer has led to an improvement in the local control and also overall survival, which has led to longer survival and higher possibility of late complications (8,9). Therefore the long term morbidity and mortality with radiotherapy has become a concern due to the doses received by the organs of risk like heart and lungs resulting in higher chances of complication while delivering radiotherapy to the thoracic region especially the left side (60). The techniques of radiotherapy have improved over the years in an attempt to decrease the doses to the OARS and thereby reducing the probability of complications.

Radiotherapy (RT) had been shown to be effective in treating breast cancer in the early twentieth century. The rationale for postmastectomy radiation is prevention of locoregional recurrence (27). Respiratory, cardiac and gastrointestinal systems effect the movement of the target during radiotherapy, among which respiratory motion has a significant effect on the intra and inter fractional treatment delivery. Hence efforts have been made to account for and counteract the same of which DIBH technique is one of the effective and reproducible methods and widely studied for breast cancer treatment (51,64,65).

Our study was performed to evaluate the efficacy of deep inspirational breath hold technique and its dosimetric advantages over free breathing technique in cardiac (heart and LAD) and ipsilateral lung sparing in left-sided postmastectomy FiF conformal radiotherapy.

The target coverage parameters (V95, V105, V107 and D_{mean}) were showed insignificant difference in our study. It was found to be 97.8 ±0.9%, 6.1 ±3.4%, 0.2 ±0.3% and 101.9 ±0.5% respectively in FB plans and 98.1 ±0.8%, 6.1 3.2%, 0.2 ±0.3%, 101.9 ±0.4% in DIBH plans respectively. In addition, the plan quality indices CI and HI were also showed 1.3 ±0.2 and 0.1 for FB plans. Similar results of 1.2 ±0.3 and 0.1 respectively were also found in DIBH plans. Overall, no difference was observed between above results.

In our study there was significant reduction in dose to heart in the DIBH plans compared to FB plans with p value of 0.0 for V5, V10, V25, V30 and D_{mean} dosimetric parameters. There was a 46% reduction in heart dose for V25 compared to the FB plan and reduction in D_{mean} in DIBH as compared to FB was 2.05 and the Dmean in DIBH was 4.78 ±2.6 Gy which was similar (5.3 ±3 Gy) to that seen in the study reported by Swamy et al. . But the data reported by Bruzzaniti et al showed very less dose for D_{mean} (1.2 Gy) for eight patients. Nissen et al also reported lower D_{mean} doses of 2.7 Gy but their study analysed the doses for DIBH and FB plans in two separate groups of patients. The dose reported for V30 Gy in the study by Swamy et al (3.3 ±7.2%) was similar to our results (4.7 ±4.6%).

The ipsilateral lung dose difference between FB and DIBH showed statistically significant p values forV5, V20, V30 and Dmean (0.015, 0.00, 0.003 and 0.00 respectively). The difference in mean doses between FB and DIBH was found to be 7%, 15.7%, 11.8% and 10.7% in V5, V20, V30 and Dmean respectively. Further, the results were similar to the results reported by swamy et al for ipsilateral lung doses. However, not much difference was reported between FB and DIBH and it was found to be insignificant (p value of 0.645) as reported in table 12 with minimum difference of 4.25% overall.

In our study there was significant reduction in dose to LAD in the DIBH plans compared to FB plans with p value of 0.0 for V5, V10, V25 and D_{mean} dosimetric parameters. There was 45.85 % reduction in heart dose for V25 compared to the FB plan and reduction in D_{mean} in DIBH as compared to FB was 8.18 Gy and the Dmean in DIBH was 9.66 ±2.6 Gy which was similar (5.3 ±3 Gy) to that seen in the study reported by Bruzzanaiti et al.

7 CONCLUSIONS

Deep inspirational breath hold technique (DIBH) resulted in significant reduction in doses to the Heart, LAD and Lungs (OARs) as with this technique there was an increase in distance between target and the OARs. With DIBH there was no compromise in doses to the target volume (PTV) with respect to coverage with no under dosage or unacceptable high doses. Radiotherapy to chest wall with the DIBH technique therefore appears to be superior to FB technique. With appropriate patient selection and adequate training, DIBH technique for radiotherapy to the chest is acceptable and achievable and therefore should be considered for all suitable patients as this could result in less radiotherapy related complications.

However this technique is time consuming as the set up is complex, results in increased time for treatment delivery, needs patient co-operation and technical expertise.

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ID NO [20] IDENTIFICATION NUMBER

NAME [ ] NAME OF THE PATIENT

HSNO [ ] HOSPITAL NUMBER

AGE [ ]

DM [ ] DIABETES

HTN [ ] HYPERTENSION

ECHO [ ]

SPIROMETRY [ ]

TB [ ] TUBERCULOSIS

ASTHMA [ ]

ANTHRACYCLINES [ ]

TAXANES [ ]

TRASTUZUMAB [ ]

TARGET(CHEST WALL + SUPRACLAV) FB = FREE BATHING DIBH =

TARGET in cc FB [ ]
TARGET in cc DIBH [ ]

ISO100% in cc FB [ ]
ISO100% in cc DIBH [ ]

V95 FB [ ]
V95 DIBH [ ]

V105 FB [ ]
V105 DIBH [ ]

V107 FB [ ]
V107 DIBH [ ]

D98 FB

D98 DIBH

D2 FB

D2 DIBH

Dmean FB

Dmean DIBH

Dmax FB

Dmax DIBH

IPSI V5 FB

IPSI V5 DIBH

IPSILATERAL LUNG

IPSI LUNG V20 FB

IPSI LUNG V20 DIBH

IPSI LUNG V30 FB

IPSI LUNG V30 DIBH

IPSI LUNG Dmean FB

IPSI LUNG Dmean DIBH

CONTRA LUNG V5 FB

CONTRA LUNG V5 DIBH

CONTRA LUNG Dmean FB

CONTRALATERAL LUNG

CONTRA LUNG Dmean DIBH

COMB LUNG V5 FB

COMB LUNG V5 DIBH

COMB LUNG V20 FB

LUNGS COMBINED

COMB LUNG V20 DIBH

COMB LUNG V30 FB

COMB LUNG V30 DIBH

COMB LUNG Dmean FB

COMB LUNG Dmean DIBH

HEART V5 FB

HEART V5 DIBH

HEART V10 FB

HEART V10 DIBH

HEART V25 FB

HEART V25 DIBH

HEART V30 FB

HEART V30 DIBH

HEART Dmean FB

HEART Dmean DIBH

LAD V5 FB

LAD V5 DIBH

LAD V10 FB

LAD V10 DIBH

LAD V25 FB

LAD V25 DIBH

LAD Dmean FB

LAD Dmean DIBH

CONTRA BREAST V5 FB

CONTRA BREAST V5 DIBH

CONTRA BREAST Dmean FB

CONTRA BREAST Dmean DIBH

CONTRA BREAST Dmax FB

CONTRA BREAST Dmax DIBH

HEART

LEFT ANTERIOR DESCENDING ARTERY

CONTRALATERAL BREAST

Informed Consent Form

Study Number: _____

Subject's Initials: _____

Subject's Name: _____

Date of Birth / Age: _____

Study Title: Dosimetric evaluation of the doses to the Heart and LAD in post mastectomy radiotherapy for left sided carcinoma breast during free breathing versus deep inspirational breath hold

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions.

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.

(iii) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published.

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s).

(v) I agree to take part in the above study.

Signature (or Thumb impression) of the Subject/Legally Acceptable

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

Study Investigator's Name: _____

Signature or thumb impression of the Witness: _____

Date: _____/_____/_____

Name & Address of the Witness: _____

Department Of Radiation Oncology, Unit II
Christian Medical College & Hospital, Vellore

Information sheet for participants

Study Title: **Dosimetric evaluation of the doses to the Heart and LAD in postmastectomy radiotherapy for left sided carcinoma breast during free breathing versus deep inspirational breath hold**

Study No :

Subject's Name :

Subject's Initial :

Date of Birth /Age :

You are being requested to participate in this study to see whether deep inspirational breath hold significantly reduces the doses to the heart and LAD in radiotherapy treatment

1.What is this study about?
This study aims to look at the reduction in doses to the heart and its blood vessel in deep inspirational breath hold technique in comparison to free breathing.

2. Why is this study being done?
The movement of chest wall during respiration can affect the radiation dose to chest wall, lung, heart and LAD. This dose variation can be significant in terms of reduction in doses to the organs at risk like heart in deep inspirational breath holding phase. Thus this study aims to document the reduction in doses to the heart and LAD in deep inspirational breath hold and free breathing.

3. What is done in the study?
In this study, patients will be trained to hold breath in deep inspiration for 15 to 20 seconds. They will then undergo planning CT scan in free breathing and deep inspirational breath hold. Further analysis will be done with the use of these CT scans.

4. What is the adverse effect from taking part in this study?
A total of 2 CT scans will be done for radiation therapy planning in the same setting. An effective dose of 7 mSv will be absorbed by the body during each

CT scan which is not significant when compared to the doses of radiation the patients would receive as a part of treatment.

5. What is the chance of you developing any study related injury?
The chance of developing study related injury is very low. Patients who will be recruited for this study are those who are planned for post mastectomy radiation therapy to left chest wall. A dose of 50 Gy in 25 fractions will be delivered to chest wall. Thus an additional radiation exposure of 7 mSv is unlikely to have any adverse effect.

6. Will you have to pay for the study?
You will have to pay for the pre radiation therapy work up, conformal planning and simulation as well as treatment charges. No additional cost will be incurred because study procedures are already included in the treatment cost.

7. What happens after the study is over?
Once the CT scans are done, you are no more part of this study. You will receive treatment as per schedule.

8. Will your personal details be kept confidential?
The results of this study might be published in a medical journal but you will not be identified by name in any publication or presentation of results. However, your medical notes may be reviewed by people associated with the study, without your additional permission, should you decide to participate in this study.

PERSONS TO CONTACT FOR FURTHER INFORMATION AND IN IMMEDIATE NEED:
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Dr Subhashini John, Department of Radiation Oncology, Christian MedicalCollege, Vellore
Dr Rajesh B , Department of Radiation Oncology, Christian Medical College, Vellore
Dr Patricia S, Department of Radiation Oncology, Christian Medical College, Vellore